IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

UNITED THERAPEUTICS CORPORATION, Plaintiff v. LIQUIDIA TECHNOLOGIES, INC., Defendant.	)	C.A. No. 23-975 (RGA) (SRF) REDACTED - PUBLIC VERSION Original filing date: August 29, 2024 Redacted filing date: September 5, 2024

JOINT CLAIM CONSTRUCTION BRIEF

MORRIS, NICHOLS, ARSHT & TUNNELL LLP
Michael J. Flynn (#5333)
1201 North Market Street
P.O. Box 1347
Wilmington, DE 19899
(302) 658-9200
mflynn@morrisnichols.com

Attorneys for Plaintiff
United Therapeutics Corporation

OF COUNSEL

William C. Jackson
Katherine Cheng
GOODWIN PROCTER LLP
1900 N St. NW
Washington, DC 20036
(202) 346-4000

Eric T. Romeo
Louis L. Lobel
GOODWIN PROCTER LLP
100 Northern Avenue
Boston, MA 02210
(617) 570-1000

Adam J. Horowitz
GOODWIN PROCTER LLP
The New York Times Building

SHAW KELLER LLP
Karen E. Keller (No. 4489)
Nathan R. Hoeschen (No. 6232)
Emily S. DiBenedetto (No. 6779)
I.M. Pei Building
1105 North Market Street, 12th Floor
Wilmington, DE 19801
(302) 298-0700
kkeller@shawkeller.com
nhoeschen@shawkeller.com
edibenedetto@shawkeller.com

Attorneys for Defendant
Liquidia Technologies, Inc.

OF COUNSEL:

Sanya Sukduang
Phillip E. Morton
Jonathan Davies
Adam Pivovar
Rachel Preston
Rosalyn D. Upton
COOLEY LLP
1299 Pennsylvania Avenue, NW, Suite 700
Washington, DC 20004-2400
(202) 842-7800

620 Eighth Avenue
New York, NY 10018
(212) 813-8800

Douglas Carsten
Art Dykhuis
Katherine Pappas
MCDERMOTT WILL & EMERY LLP
18565 Jamboree Road, Suite 250
Irvine, CA 92615
(949) 851-0633

Lauren Strosnick
Kyung Taeck Minn
COOLEY LLP
3175 Hanover Street
Palo Alto, CA 94304-1130
(650) 843-5000

August 29, 2024

TABLE OF CONTENTS

TABLE OF AUTHORITIES ii
TABLE OF EXHIBITS IN JOINT APPENDIX v
I. INTRODUCTION 1
A. Plaintiff's Opening Position 1
B. Defendant's Answering Position 2
C. Plaintiff's Reply Position 2
II. LEGAL STANDARD 3
A. Defendant's Position 3
III. PERSON OF ORDINARY SKILL IN THE ART 4
A. Plaintiff's Opening Position 4
B. Defendant's Answering Position 4
IV. REPRESENTATIVE CLAIMS 4
A. Claim 1 4
B. Claim 2 4
C. Claim 11 5
D. Claim 14 5
V. AGREED-UPON CONSTRUCTIONS 5
A. Preamble (claim 1) 5
VI. DISPUTED CONSTRUCTIONS 5
A. "a"/"the" (claims 1-5, 8-10, 15-19) 5
1. Plaintiff's Opening Position 6
2. Defendant's Answering Position 8
3. Plaintiff's Reply Position 11
4. Defendant's Sur-Reply Position 16
B. "maximum tolerated dose" (claim 1) 18
1. Plaintiff's Opening Position 18
2. Defendant's Answering Position 25
3. Plaintiff's Reply Position 33
4. Defendant's Sur-Reply Position 37
C. "pulsed inhalation device" (claims 11, 14) 40
1. Plaintiff's Opening Position 41
2. Defendant's Answering Position 46
3. Plaintiff's Reply Position 51
4. Defendant's Sur-Reply Position 57

TABLE OF AUTHORITIES

Page(s)

Cases

01 Communique Lab., Inc. v. LogMeIn, Inc.,
687 F.3d 1292 (Fed. Cir. 2012).....12, 17

ABS Glob., Inc. v. Cytonome/St, LLC,
84 F.4th 1034 (Fed. Cir. 2023) 7, 8

Abtox, Inc. v. Exitron Corp.,
122 F.3d 1019 (Fed. Cir. 1997), *opinion amended on reh'g*,
131 F.3d 1009 (Fed. Cir. 1997).....9, 13, 14, 17

Align Tech., Inc. v. 3Shape,
2021 WL 2320139 (D. Del. June 7, 2021).....55

Azurity Pharms., Inc. v. Alkem Labs. Ltd,
2021 WL 5332406 (D. Del. Nov. 16, 2021) ..... *passim*

Baldwin Graphic Sys., Inc. v. Siebert, Inc.,
512 F.3d 1338 (Fed. Cir. 2008).....7, 8, 13, 17

BASF Corp. v. Johnson Matthey Inc.,
875 F.3d 1360 (Fed. Cir. 2017).....23, 36

Bial-Portela & CA. S.A. v. Alkem Labs. Ltd.,
2022 WL 4244989 (D. Del. Sept. 15, 2022).....56

Biovail Corp. Int'l v. Andrx Pharm., Inc.,
239 F.3d 1297 (Fed. Cir. 2001).....52

Blazer v. Best Bee Bros. LLC,
2022 WL 16954848 (Fed. Cir. 2022).....12

CUPP Computing AS v. Trend Micro Inc.,
53 F.4th 1376 (Fed. Cir. 2022) 54

Dow Chem. Co. v. Nova Chems. Corp. (Canada),
803 F.3d 620 (Fed. Cir. 2015).....25, 33, 39

Elekta Instrument S.A. v. O.U.R. Sci. Int'l, Inc.,
214 F.3d 1302 (Fed. Cir. 2000).....50

Epistar Corp. v. Int'l Trade Comm'n,
566 F.3d 1321 (Fed. Cir. 2009).....2

Exeltis USA, Inc. v. Lupin Ltd.,
No. 22-434-RGA, 2023 WL 2306736 (D. Del. Mar. 1, 2023) (Andrews, J.).....9

Genentech, Inc. v. Chiron Corp.,
112 F.3d 495 (Fed. Cir. 1997).....14

Genuine Enabling Tech. LLC v. Nintendo Co., Ltd.,
29 F.4th 1365 (Fed. Cir. 2022) 46

Hyperphrase Techs., LLC v. Google, Inc.,
260 F. App'x 274 (Fed. Cir. 2007) 9, 14

InterDigital Commc'ns, LLC v. Int'l Trade Comm'n,
690 F.3d 1318 (Fed. Cir. 2012).....46

Jack Guttman, Inc. v. Kopykake Enters., Inc.,
302 F.3d 1352 (Fed. Cir. 2002).....9

KCJ Corp. v. Kinetic Concepts, Inc.,
223 F.3d 1351 (Fed. Cir. 2000).....7

Liebel-Flarsheim Co. v. Medrad, Inc.,
358 F.3d 898 (Fed. Cir. 2004).....52

Lite-Netics, LLC v. Nu Tsai Cap. LLC,
60 F.4th 1335 (Fed. Cir. 2023) 7, 8

Markman v. Westview Instruments, Inc.,
517 U.S. 370 (1996).....3

Merck & Co. v. Teva Pharms. USA, Inc.,
395 F.3d 1364 (Fed. Cir. 2005).....49, 57

Nautilus, Inc. v. Biosig Instruments, Inc.,
572 U.S. 898 (2014).....23, 25, 29

Network Com., Inc. v. Microsoft Corp.,
422 F.3d 1353 (Fed. Cir. 2005).....55, 56

Nexeon Ltd. v. EaglePicher Techs. LLC,
2018 WL 1942199 (D. Del. Apr. 25, 2018).....42

Oatey Co. v. IPS Corp.,
514 F.3d 1271 (Fed. Cir. 2008).....45

Osram GmbH v. Int'l Trade Comm'n,
505 F.3d 1351 (Fed. Cir. 2007).....45, 54

Otsuka Pharm. Co. v. Lupin Ltd.,
2022 WL 2952759 (D. Del. July 26, 2022) 54

Pacira Pharms., Inc. v. eVenus Pharms. Labs., Inc.,
2023 WL 3841559 (D.N.J. June 6, 2023) 13, 17

Pfizer Inc. v. Alkem Labs. Ltd.,
2014 WL 12798743 (D. Del. Dec. 2, 2014).....52

Phillips v. AWH Corp.,
415 F.3d 1303 (Fed. Cir. 2005).....3, 19, 45, 46

Process Control Corp. v. HydReclaim Corp.,
190 F.3d 1350 (Fed. Cir. 1999).....50

SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc.,
242 F.3d 1337 (Fed. Cir. 2001).....12

Sonix Tech. Co., Ltd. v. Publ'ns Int'l, Ltd.,
844 F.3d 1370 (Fed. Cir. 2017).....24

Sonrai Memory Ltd. v. Kingston Tech. Co., Inc.,
2022 WL 3640302 (W.D. Tex. Aug. 23, 2022) 24

Teva Pharms. USA, Inc. v. Sandoz, Inc.,
789 F.3d 1335 (Fed. Cir. 2015).....25, 33, 37, 39

Trustees of Columbia Univ. v. Symantec Corp.,
811 F.3d 1359 (Fed. Cir. 2016).....3

TVIIM, LLC v. McAfee, Inc.,
851 F.3d 1356 (Fed. Cir. 2017).....11

Verizon Servs. Corp. v. Vonage Holdings Corp.,
503 F.3d 1295 (Fed. Cir. 2007).....45

Vitronics Corp. v. Conceptronic, Inc.,
90 F.3d 1576 (Fed. Cir. 1996).....31

White v. Dunbar,
119 U.S. 47 (1886).....51

TABLE OF EXHIBITS IN JOINT APPENDIX

Ex.	Description
1	Liquidia's Initial Invalidity Contentions (excerpt)
2	*United Therapeutics Corp., v. Liquidia Tech., Inc.*, C.A. No. 20-755-RGA-JLH, D.I. 405 (D. Del. Mar. 31, 2022) ('793 Trial Tr., Day 4) (excerpt)
3	2009 Tyvaso® Label
4	2004 Remodulin® Label
5	Liquidia's June 20, 2022, Corporate Overview (excerpt)
6	Liquidia's 2018 Form 10-K (excerpt)
7	Liquidia's 2019 Form 10-K (excerpt)
8	Proposed Yutrepia™ Label (2024)
9	Preliminary Injunction Hearing Transcript (April 23, 2024) (excerpt)
10	R. Barst, et al., Clinical perspectives with long-term pulsed inhaled nitric oxide for the treatment of pulmonary arterial hypertension, *Pulmonary Circulation* 2:139 (2012)
11	C. Lee et al., Practical considerations in the management of inhaled prostacyclin therapy for pulmonary hypertension associated with interstitial lung disease (WHO group 3), *Respiratory Med.* 196 (2022)
12	U.S. Patent Application Publication No. US 2008/0200449 A1 (LIQ_PH-ILD_00101769)
13	U.S. Patent No. 9,358,240 (LIQ_PH-ILD_00101827)
14	U.S. Patent No. 9,339,507 (LIQ_PH-ILD_00101803)
15	U.S. Patent No. 10,376,525 (LIQ_PH-ILD_00101719)
16	U.S. Patent No. 10,716,793 (UTC_PH-ILD_009772)
17	Definition of "Pulse", Merriam-Webster Dictionary (October 23, 2019), available at https://web.archive.org/web/20191023091508/https://www.mer-riam- webster.com/dictionary/pulse (LIQ_PH-ILD_00102183)
18	Tyvaso Inhalation System, Instructions for Use Manual (LIQ_PH-ILD_00002547)
19	Transcript from the March 10, 2024 Deposition of Steven D. Nathan, M.D. (LIQ_PH-ILD_00000677)
20	International Publication No. WO 2017/192993 A1 (LIQ_PH-ILD_00102194)
21	International Publication No. WO 2019/237028 A1 (LIQ_PH-ILD_00102338)
22	Liquidia's First Amended Invalidity Contentions (excerpt)
23	Transcript from the April 6, 2024 Deposition of Richard Channick, M.D.
24	Letter from Liquidia to UTC (Aug. 2, 2024)
25	U.S. Patent No. 10,786,482
26	OPTINEB®-ir Operating Instructions (LIQ_PH-ILD_00002406)
27	VENTA-NEB-ir A-I-C-I Operating Instructions (LIQ_PH-ILD_00002935)

I. INTRODUCTION

A. Plaintiff's Opening Position

Pulmonary hypertension ("PH") is a life-threatening disease characterized by elevated blood pressure in the vasculature of the lungs. There are different forms of PH, including pulmonary arterial hypertension ("PAH") and PH associated with interstitial lung disease ("PH-ILD"). D.I. 26 (UTC PI Motion) at 2-3. Because the causes of different forms of PH vary, so do the treatments. *Id.* And before UTC's[1] INCREASE clinical trial, treprostinil treatments were approved for the treatment of PAH only. After INCREASE, two treprostinil treatments, Tyvaso® and Tyvaso DPI®, became the first products approved for the treatment of PH-ILD. *Id.*

Following the INCREASE trial, the USPTO issued UTC's U.S. Patent No. 11,826,327 (the "'327 patent"), which is directed to methods of improving exercise capacity in a patient having PH-ILD by administering treprostinil via inhalation. The '327 patent's asserted claims reflect the dosing administration regime and clinical trial information described in the patent itself, which shows improvements in exercise capacity, 6 minute walk distance, forced vital capacity, and other characteristics.

The three terms raised for construction—"a"/"the," "maximum tolerated dose," and "pulsed inhalation device"—were all proposed by Liquidia. UTC disagrees that these terms require any construction because their meanings would be readily apparent to the person of ordinary skill in the art ("POSA") as of the priority date. Nonetheless, because Liquidia raised these terms, UTC has proposed constructions that are grounded in the '327 patent's claims, specification, and other relevant intrinsic evidence. Liquidia's proposed constructions depart from the intrinsic evidence, represent an improper attempt to manufacture non-infringement and invalidity defenses, and

[1] "UTC" refers to Plaintiff United Therapeutics Corporation. "Liquidia" refers to Defendant Liquidia Technologies, Inc.

should be rejected. To the extent the Court decides to construe the three terms under dispute, it should adopt UTC's proposed constructions.

B. Defendant's Answering Position

Liquidia filed an NDA under § 505(b)(2) of the Federal Food, Drug, and Cosmetic Act seeking FDA approval to market YUTREPIA®, its novel inhaled dry-powder formulation of treprostinil for the treatment of pulmonary hypertension associated with interstitial lung disease ("PH-ILD"). D.I. 1 (Complaint), ¶ 3. Although UTC originally asserted two patents, only one is at issue in this case—U.S. Patent No. 11,826,327 (the "'327 patent"). To justify maintaining its infringement allegations, UTC now seeks broad constructions of the disputed phrases despite lacking support from the intrinsic evidence. Liquidia's proposed constructions, by contrast, are fully supported by the intrinsic evidence, warranting their adoption.

C. Plaintiff's Reply Position

None of Liquidia's proposed terms require construction. It is Liquidia's burden alone to convince the Court that the terms "a"/"the," "maximum tolerated dose," and "pulsed inhalation device" must be redefined. *See Epistar Corp. v. Int'l Trade Comm'n*, 566 F.3d 1321, 1334-37 (Fed. Cir. 2009) (emphasizing that there is "a heavy presumption that claim terms carry their full ordinary and customary meaning, unless it can [be] show[n] th[at] patentee expressly relinquished claim scope").

Liquidia has failed to meet that burden for any of the terms at issue. Although Liquidia asserts that "UTC now seeks broad constructions," allegedly "[t]o justify maintaining its infringement allegations," it was *Liquidia* that proposed every term at issue for construction. Every term is a flawed attempt to create defenses to Liquidia's infringement by redefining the words chosen by the inventors.

For "a"/"the," Liquidia seeks to redefine basic articles in the English language—contrary to the Federal Circuit's rule regarding interpreting those words—even though the POSA and laypersons easily understand those terms, all in the name of supporting alleged "invalidity positions Liquidia intends to take." *Infra* § VI.A, at 5-6. For "maximum tolerated dose," Liquidia again tries to manufacture an invalidity position based on misunderstanding a term consistently used and understood in the patent, literature, and in clinical practice. And for "pulsed inhalation device," Liquidia seeks to import a limitation *from extrinsic evidence* to create a non-infringement defense.

Liquidia's proposed constructions are unjustified. The POSA would readily understand the terms at issue, and even if Liquidia's proposed constructions are adopted, the claims would still be infringed, so there is no need to construe the terms. To the extent the Court construes any of the terms, UTC's constructions are consistent with the intrinsic evidence and the terms' plain and ordinary meanings and should be adopted.

II. LEGAL STANDARD

A. Defendant's Position

Claim construction is a question of law. *See Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 384 (1996). The ultimate question when construing claims is how a person of ordinary skill in the art understand the claim term in the context of the specification. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005). While claim construction always begins with an analysis of the claim language, "claims must be read in view of the specification . . . ." *Trustees of Columbia Univ. v. Symantec Corp.*, 811 F.3d 1359, 1362–63 (Fed. Cir. 2016) (citation omitted). A court may also consider the patent's prosecution history and dictionary definitions that are consistent with the definitions provided in the patent. *See id.*

III. PERSON OF ORDINARY SKILL IN THE ART

A. Plaintiff's Opening Position

The '327 patent is directed to methods of improving exercise capacity in a patient having PH-ILD. The POSA would have a graduate degree in medicine or a field relating to drug development, such as an M.D. or a Ph.D., with at least two years' experience treating patients with interstitial lung disease, including with PH-ILD. D.I. 26 at 6.

B. Defendant's Answering Position

A person of ordinary skill in the art ("POSA") would have a medical degree with a specialty in pulmonology or cardiology, plus at least two years of experience treating patients with PH as an attending, including PH-ILD and including with inhaled therapies, or equivalent degree or experience. *See* D.I. 54, ¶ 24.

IV. REPRESENTATIVE CLAIMS[2]

A. Claim 1

> A method of improving exercise capacity in ***a*** patient having pulmonary hypertension associated with interstitial lung disease, comprising administering by inhalation to ***the*** patient having pulmonary hypertension associated with interstitial lung disease an effective amount of at least 15 micrograms up to ***a maximum tolerated dose*** of treprostinil or a pharmaceutically acceptable salt thereof in ***a*** single administration event that comprises at least 6 micrograms per breath.

B. Claim 2

> The method of claim 1, wherein said administering provides a statistically significant increase of a 6 minutes walk distance in ***the*** patient after 8 weeks, 12 weeks, or 16 weeks of ***the*** administering.

[2] Pursuant to the Scheduling Order, the terms that Liquidia proposes this Court construe are italicized. D.I. 45, ¶ 7 n.2.

C. Claim 11

> The method of claim 1, wherein said administering is performed by a ***pulsed inhalation device***.

D. Claim 14

> The method of claim 11, wherein the ***pulsed inhalation device*** is a dry powder inhaler comprising a dry powder comprising treprostinil or a pharmaceutically acceptable salt thereof.

V. AGREED-UPON CONSTRUCTIONS

A. Preamble (claim 1)

The parties agree that the preamble of claim 1—"[a] method of improving exercise capacity in a patient having pulmonary hypertension associated with interstitial lung disease"—is limiting. Thus, the parties request that the Court adopt their agreed-upon construction.

VI. DISPUTED CONSTRUCTIONS

A. "a"/"the" in the following terms:
"a patient,"
"the patient,"
"a maximum tolerated dose,"
"a single administration event,"
"the administering," and
"the single inhalation administration event"
(claims 1-5, 8-10, 15-19)

Plaintiff's Proposed Construction	**Defendant's Proposed Construction**
No construction necessary. To the extent the term is construed, "a"/"the" should be construed to have its plain and ordinary meaning in view of the specification, which is: "one or more unless context clearly dictates otherwise"	"one and more than one"
From Liquidia's Invalidity Contentions, UTC understands that Liquidia wants to construe	The construction of "a" and "the" with the associated terms relates to invalidity positions

Plaintiff's Proposed Construction	Defendant's Proposed Construction
this term to somehow help support § 112 defenses it raises relating to dependent claims 2, 4, 9, and 10. Resolution of this dispute hardly matters, if at all, given the narrow dispute—whether the POSA must consider context—because the claims are valid under either construction.	Liquidia intends to take and in particular § 112 written description, enablement, and indefiniteness.

1. Plaintiff's Opening Position

The terms "a" and "the" do not require construction. Both the POSA and laypersons would understand the meaning of the commonly used articles "a" and "the." The specification describes the meaning of these terms, and construction will not be helpful to the Court or jury.

This is especially true when Liquidia has all but agreed to UTC's conditional proposed construction. Liquidia's initial construction was "one *and* more than one," but Liquidia's Invalidity Contentions subsequently (and without explanation) revised that construction to "one *or* more than one." D.I. 94, Ex. A (Joint Claim Construction Chart ("JCCC"))[3] at 5-6 (emphasis added); Ex. 1 (Invalidity Contentions) at 158 (emphasis added). Because Liquidia's revised stance uses the word "or" and thus matches UTC's construction, it is unclear what dispute, if any, remains.

To the extent "a"/"the" requires construction, it should be understood according to its plain and ordinary meaning in view of the Federal Circuit's general rule and the specification, which is "one or more unless context clearly dictates otherwise." D.I. 94 (JCCC Ex. B) ('327 patent) at 6:15-17.

[3] Unless otherwise noted, citations to lettered Exhibits refer to exhibits to the JCCC, and citations to pages of lettered Exhibits A and C refer to the blue ECF pages numbers at the top of each page.

(i) If construction is necessary, UTC proposes the plain and ordinary meaning for "a"/"the."

The Federal Circuit and courts in this District have repeatedly and consistently recognized the "general rule" that "a," especially when used in open-ended "comprising" claims—like those asserted here—means one or more unless the context clearly dictates otherwise. *See, e.g.*, *ABS Glob., Inc. v. Cytonome/St, LLC*, 84 F.4th 1034, 1040 (Fed. Cir. 2023) ("[U]se of 'a' . . . before a noun naming an object requires that the phrase be construed to mean 'one or more' unless the context sufficiently indicates otherwise." (quotation omitted)); *Lite-Netics, LLC v. Nu Tsai Cap. LLC*, 60 F.4th 1335, 1345 (Fed. Cir. 2023) (same); *KCJ Corp. v. Kinetic Concepts, Inc.*, 223 F.3d 1351, 1356 (Fed. Cir. 2000) ("This court has repeatedly emphasized that an indefinite article 'a' . . . in patent parlance carries the meaning of 'one or more' in open-ended claims containing the transitional phrase 'comprising.'"); *Baldwin Graphic Sys., Inc. v. Siebert, Inc.*, 512 F.3d 1338, 1342 (Fed. Cir. 2008) ("That 'a' . . . can mean 'one or more' is best described as a rule, rather than merely as a presumption or even a convention."); *Azurity Pharms., Inc. v. Alkem Labs. Ltd*, 2021 WL 5332406, at *3 (D. Del. Nov. 16, 2021) ("As a general rule, the word[] 'a' . . . in a patent claim carr[ies] the meaning of 'one or more.'"). In fact, in the prior litigation between the parties, this Court also recognized that "one or more is simply the prefer[red] reading" of "a." Ex. 2 ('793 Trial Tr., Day 4) at 937:6-938:16.

Consistent with the Federal Circuit's general rule, the '327 patent expressly defines "a"/"the" as follows: "as used herein and in the appended claims, the singular forms 'a,' 'an,' and 'the' include plural referents unless the context clearly dictates otherwise." Ex. B ('327 patent) at 6:15-17. UTC's proposed construction adopts this meaning and is consistent with the Federal Circuit's general rule regarding the plain and ordinary meaning of these terms. *See ABS Glob.*, 84 F.4th at 1040-41 (finding that the specification's express "definition reinforces, rather than

negates, the applicability here of the 'one or more' general rule concerning 'a'"). "An exception to the general rule that 'a' or 'an' means more than one only arises where the language of the claims themselves, the specification, or the prosecution history necessitate a departure from the rule." *Baldwin Graphic Sys.*, 512 F.3d at 1342-43; *see also ABS Glob.*, 84 F.4th at 1041 ("It also brings into play the lexicography principle—that, with narrow exceptions, where the specification instructs as to the meaning of a claim term, the inventor's lexicography governs."). The specification and the Federal Circuit's general rule are in accord: "a"/"the" means "one or more unless context dictates otherwise."

(ii) Liquidia's proposed construction only selectively credits the specification.

The only substantive difference between Liquidia's current construction and UTC's is that Liquidia excludes the specification's phrase, "unless context clearly dictates otherwise." Refusing to include that phrase, however, ignores express instructions from both the inventors and the Federal Circuit that context matters when determining whether the singular or plural (or both) forms of these terms should be applied. Ex. B ('327 patent) at 6:15-17; *Lite-Netics*, 60 F.4th at 1345. To the extent Liquidia reverts to its previous construction ("one *and* more than one"), that construction is plainly at odds with both the inventors' definition and the Federal Circuit's "general rule," discussed above. *See supra* § VI.A.1 at 7-8. If the Court opts to construe "a"/"the," the Court should reject Liquidia's proposed construction and adopt UTC's.

2. Defendant's Answering Position

Liquidia's proposed construction for "a"/"the" to mean "one and more than one" is consistent with the '327 patent's specification.[4] The '327 patent provides, and UTC cites to, the

[4] UTC points out that Liquidia's Initial Invalidity Contentions put forth the construction "one or more than one" for the term "a"/"the". *See* Opening Br., 6. This is an inadvertent typographical

passage: "as used herein and in the appended claims, the singular forms 'a,' 'an,' and 'the' **include** plural referents unless context clearly dictates otherwise." '327 patent, 6:15-17 (emphasis added); Opening Br., 7.[5] And UTC admits in its Opening Claim Construction Brief ("Opening Br.") that the '327 patent "expressly defines" the terms "a"/"the" using the language cited above. Opening Br., 7. Because the '327 patent applicant could have opted for language such as "may include," but instead settled on the unmodified term "include," the applicant intended for "a," "an," and "the" to encompass both the singular and plural rather than optionally one or the other. "Where, as here, the patentee has clearly defined a claim term, that definition usually is dispositive; it is the single best guide to the meaning of a disputed term." *Jack Guttman, Inc. v. Kopykake Enters., Inc.*, 302 F.3d 1352, 1360–61 (Fed. Cir. 2002) (internal quotation marks omitted) (citation omitted); *see also Exeltis USA, Inc. v. Lupin Ltd.*, No. 22-434-RGA, 2023 WL 2306736, at *5–6 (D. Del. Mar. 1, 2023) (Andrews, J.) (applying the specification's definition of "about" and finding that the specification's definition rendered the claim indefinite). The Federal Circuit has made clear that when considering the construction of "a"/"the," the intrinsic evidence controls. *See*, *Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019, 1023–24 (Fed. Cir. 1997) (construing "a metallic gas confining chamber" as limited to a single chamber because "[n]othing in the written description suggests that the claim language encompasses a device with more than one gas-confining chamber"), *opinion amended on reh'g*, 131 F.3d 1009 (Fed. Cir. 1997); *see also Hyperphrase Techs., LLC v. Google,*

---

error and Liquidia has served its First Amended Invalidity Contentions on July 16, 2024 to correct this error. To be clear, Liquidia proposed in the Joint Claim Construction Chart that "a"/"the" be construed as "one and more than one," and does not, and never did, intend to change its proposed construction. D.I. 94 at 2.

[5] Defendant's citations in its answering and sur-reply positions to "Opening Br.," "Response," and "Reply" are to Plaintiff's Opening Position, Defendant's Answering Position, and Plaintiff's Reply Position, respectively. The page number following the citations to "Opening Br.," "Response," and "Reply" are to the page numbers in this Joint Claim Construction Brief, and not to the page numbers of the opening, answering, and reply briefs that were exchanged between the parties.

Inc., 260 F. App'x 274, 279 (Fed. Cir. 2007) (nonprecedential) ("the use of the singular form 'a' in conjunction with 'comprising' and without narrowing language, such as 'one and only one,' typically encompasses **both** singular and plural possibilities.") (emphasis added). Here, because the intrinsic evidence unequivocally defined "a"/"the" to "include" the plural as well as the singular, and the asserted claims use the "comprising" transitional phrase, construction of "a" and "the" must also include both, leading to Liquidia's construction: "one and more than one." In contrast, UTC's construction disregards this intrinsic evidence by rendering the singular and plural as optional: "one ***or*** more unless context clearly dictates otherwise." UTC's construction disregards the "includes" language of the '327 patent specification and should be rejected.

UTC urges consideration of the phrase, "unless context clearly dictates otherwise," and argues that "context matters when determining whether the singular or plural (or both) forms of these terms should be applied." Opening Br., 8. Liquidia does not disagree that context matters, but here, the context of the specification and claims dictates that "a"/ "the" in the asserted claims include both the singular and the plural. Most clearly, asserted claim 1 of the '327 patent is directed to "[a] method of improving exercise capacity in a **patient** having pulmonary hypertension associated with interstitial lung disease, comprising administering by inhalation to the **patient** having pulmonary hypertension associated with interstitial lung disease[.]" '327 patent, cl. 1 (emphasis added). And all other asserted claims depend directly or indirectly from claim 1. *See id.* at cls. 1–11, 14–19. While the INCREASE study, which allegedly formed the basis of the '327 patent disclosure (*see* Ex. 9 (D.I. Apr. 23, 2024 PI Hr'g Tr.) at 8:7-10), treated individual patients but aggregated data for statistical analysis, doctors in the United States would be treating PH-ILD patients with inhaled treprostinil on an individual patient-by-individual patient basis without aggregating statistical data. *See* D.I. 52, Ex. 23 (INCREASE study aggregating treatment data from

326 patients). Thus, the asserted claims necessarily cover both the treatment of a single patient with PH-ILD and the treatment of multiple patients with PH-ILD. Adopting UTC's construction would make the infringement inquiry untenable as it would require "context" in each instance to determine whether an action is, or is not, infringing.

To the extent UTC argues that in the context of asserted claims 2, 4, 6, 7, and 9, all of which require a "statistically significant" result, the plural form of "a"/"the" must apply, such a construction would exclude the treatment of a single patient. That is, under UTC's proposed construction of "a"/"the", claims 2, 4, 6, 7, 9, and 10 could only be infringed if (1) a doctor treats multiple PH-ILD patients; (2) aggregates the treatment results for the patients; and (3) performs a statistical analysis to determine whether a statistically significant result was achieved. UTC, however, would still assert Liquidia induces infringement of those claims even if one doctor treats a single PH-ILD patient. UTC cannot offer a construction that excludes a treating a single PH-ILD patient to preserve the validity of certain claims, but then asserts that treatment of a single PH-ILD patient would nonetheless infringe that same claim, as claim terms must be constructed the same for infringement and validity. *TVIIM, LLC v. McAfee, Inc.*, 851 F.3d 1356, 1362 (Fed. Cir. 2017) ("[c]laim terms must be construed the same way for the purpose of determining invalidity and infringement"). Liquidia's proposed construction for "a"/"the" is consistent with the claims and specification of the '327 patent and should be adopted.

3. Plaintiff's Reply Position

Liquidia's proposal to construe the terms "a" and "the" as always meaning "one *and* more than one" is improper. *Supra* § VI.A.2, at 8-9 (emphasis added). Liquidia's construction is not only contrary to the specification and binding case law, but its selective interpretation also defies

the natural reading of the claims.[6] Liquidia says its proposed construction is required "[b]ecause the '327 patent applicant could have opted for language such as 'may include,' but instead settled on the unmodified term 'include[.]'" *Id.* at 9. Liquidia's attempt to narrow the claims in this way has been "described as one of the cardinal sins of patent law." *Blazer v. Best Bee Bros. LLC*, 2022 WL 16954848, at *4 (Fed. Cir. 2022) (citing *SciMed Life Sys., Inc. v. Advanced Cardiovascular Sys., Inc*., 242 F.3d 1337, 1340 (Fed. Cir. 2001)) (internal quotations omitted).

The terms "a" and "the" would be readily understood by the POSA. However, to the extent construction is required, UTC's proposal—"one or more unless context clearly dictates otherwise"—is consistent with both the specification and the relevant precedent at the Federal Circuit and in this District. The only precedent Liquidia cites in support of its construction relates to lexicography, but Liquidia identifies no place where "the patentee has clearly defined" a/the in the claims to "encompass both the singular and plural rather than optionally one or the other." *Supra* § VI.A.2, at 9 (emphasis added). To the contrary, the inventors made clear in the specification that "a"/"the" may optionally be both singular and plural, stating that "in the appended claims, the singular forms 'a,' 'an,' and 'the' include plural referents unless the context clearly dictates otherwise." Ex. B ('327 patent) at 6:15-17 (emphasis added). Liquidia's proposed construction therefore directly conflicts with the plain language of the specification, which Liquidia admits "is the single best guide to the meaning of a disputed term." *Supra* § VI.A.2, at 9.

Liquidia's position is in direct tension with governing case law. *Supra* § VI.A.1, at 7. Precedent makes clear that, even more than a "presumption," there is a "rule" that "the words 'a' or 'an' in a patent claim carry the meaning of 'one or more.'" *01 Communique Lab., Inc. v.*

[6] Liquidia asserts that the terms "a"/"the" require construction for claims 1-5, 8-10, and 15-19, but Liquidia is silent regarding several other instances of those same claim terms. *Compare* Ex. A (JCCC) at 2-3 *and* Ex. B ('327 patent) at claims 1-11 and 14-19 *with supra* § VI.A.2, at 8-11.

LogMeIn, Inc., 687 F.3d 1292, 1297 (Fed. Cir. 2012) (internal quotations omitted); *Baldwin*, 512 F.3d at 1342. This rule applies "even more strongly[] in the 'comprising' claims." *Azurity*, 2021 WL 5332406, at *3. "The exceptions to this rule are extremely limited: a patentee must evince a clear intent to limit 'a' or 'an' to 'one[]' . . . [and] only arise[] where the language of the claims themselves, the specification, or the prosecution history *necessitate* a departure from the rule."[7] *Baldwin*, 512 F.3d at 1342-43 (emphasis added) (internal quotations omitted). Notably, every claim in the '327 patent uses the "comprising" transitional phrase. Liquidia's attorney argument—which directly conflicts with Federal Circuit precedent—fails to prove that the claims "necessitate" a wholesale departure from the plain text of the specification and the Federal Circuit's accepted rule. *See id.*

An almost identical dispute occurred in this District's recent *Azurity* case, where the parties disputed the meaning of the term "a," and the specification stated that "[a]s used herein and in the appended claims, the singular forms 'a', 'an', and 'the' include plural reference unless the context clearly dictates otherwise." *Azurity*, 2021 WL 5332406, at *3-7. The court held that "there is nothing in the claims, specification, or prosecution history that warrants a departure from the general rule that 'a' means 'one or more.'" *Id.* at *5; *see also Pacira Pharms., Inc. v. eVenus Pharms. Labs., Inc.*, 2023 WL 3841559, at *12-13 (D.N.J. June 6, 2023) (emphasizing the "conventional rule" that the "article 'a' or 'an' in patent parlance carries the meaning of 'one or more' in open-ended claims containing the transitional phrase 'comprising'"). The same is true here.

Liquidia's cases (*supra* § VI.A.2, at 9-10) do not support its argument and instead support the Federal Circuit's general rule. *Abtox* involved a device claim directed to "a metallic gas-

[7] UTC's proposed construction acknowledges this "exception," whereas Liquidia's does not.

confining chamber" where "[n]othing in the written description suggest[ed] that the claim language encompasses a device with more than one gas-confining chamber." *Abtox,* 122 F.3d at 1023-24. In contrast, the claims of the '327 patent are directed to methods of treatment, which Liquidia admits "necessarily *cover* both the treatment of a single patient with PH-ILD and the treatment of multiple patients with PH-ILD." *Supra* § VI.A.2, at 10-11 (emphasis added). That is because the claims were drafted using the transitional phrase "comprising," not because of how the inventors defined "a" and "the."

Likewise, *Hyperphrase* held that "the singular form 'a' in conjunction with 'comprising' and without narrowing language, such as 'one and only one,' typically encompasses both singular and plural *possibilities*." *Hyperphrase Techs.*, 260 F. App'x at 279 (emphasis added). Claim 1—a comprising claim—therefore covers both possibilities of treating a single patient or multiple patients. But these cases do not require that both possibilities simultaneously exist. *See also Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501 (Fed. Cir. 1997) ("'Comprising' is a term of art used in claim language which means that the named elements are essential, but other elements *may be* added and still form a[n embodiment] within the scope of the claim.") (emphasis added). Liquidia fails to argue, much less provide evidence, that "a" and "the" in claims 1-5, 8-10, and 15-19 must *always* and *simultaneously* mean treating both a single patient *and* multiple patients.

Liquidia attempts to nitpick the specification—not the claims—by complaining that the inventors' choice to use "include" rather than "may include" means that "a" and "the" must *always* be read as simultaneously plural or singular. *Supra* § VI.A.2, at 8-9 (citing '327 patent at 6:15-17). But this ignores the very next phrase in the specification—"unless the context clearly dictates

otherwise"—which makes clear that context matters.[8] Ex. B ('327 patent) at 6:15-17. In fact, as discussed above, an almost identical specification passage using "include" was examined in *Azurity*, and the court nonetheless construed "a" to mean "one or more." 2021 WL 5332406, at *3-7. Liquidia has pointed to no evidence that would compel a different result here.

Liquidia has failed to explain why construing "a" and "the" is necessary. Liquidia's own initial invalidity contentions conceded that the proper construction of "a"/"the" is "one *or* more than one." Ex. 1 (Liquidia's Initial Invalidity Contentions) at 158 (emphasis added). That party admission—which is consistent with the claims, specification, and general accepted rule—should control. Liquidia has amended its contentions and now attempts to cast this statement as "an inadvertent typographical error." *Supra* § VI.A.2, at 8 n.4. Liquidia made no other edits to its contentions that might explain how this construction affects Liquidia's invalidity analysis, if it does at all. Ex. 22 (First Amended Invalidity Contentions) at 158. Liquidia similarly fails to explain how its proposed construction impacts invalidity, as it merely argues that "UTC cannot offer a construction that *excludes* a [sic] treating a single PH-ILD patient to preserve the validity of certain claims . . . ." *Supra* § VI.A.2, at 8-11 (emphasis added). But it is Liquidia that seeks to "exclude" treating a single patient by requiring "a"/"the" to be construed as "one *and* more than one," whereas UTC's construction allows "one or more."

Finally, Liquidia argues (*supra* § VI.A.2, at 11) that UTC's proposed construction requires that a doctor (1) treats multiple patients, (2) aggregates those results, and (3) performs a statistical analysis on the treated patients. That is plainly wrong. For example, claim 2 does not require a

[8] Liquidia says it "does not disagree that context matters" but in the same sentence states that the specification and claims "dictates" [sic] that "the asserted claims include both the singular and plural." *Supra* § VI.A.2, at 10. This facially inconsistent position finds no support in either fact or law.

doctor to treat multiple patients and aggregate data from those patients for UTC to prove infringement of that claim. Liquidia's interpretation of the claims is incorrect and unsupported, adds several limitations not found in the claims, and is not mandated by the plain and ordinary meaning of "a" or "the."

* * *

Liquidia's proposed construction of "a"/"the" should be rejected. To the extent the Court construes "a"/"the," it should adopt UTC's proposed construction.

4. Defendant's Sur-Reply Position

The inventors did not make clear, as UTC contends, that "'a'/'the' may optionally be both singular and plural[.]" *See* Reply, 12. Instead, the inventors stated that "the singular forms … ***include*** plural referents[,]" not that the singular forms ***optionally*** include plural referents. '327 patent, 6:15-17 (emphasis added). That UTC wants the specification to make singular and plural "optional" does not make it so.

UTC cites to the *Azurity* case where the court held that nothing in the intrinsic evidence warranted a departure from "a"/"the" meaning "one or more." Reply, 13. *Azurity* is factually distinct because the issue there was whether the claims were limited to only one buffer. The patent specification in *Azurity* expressly stated that "for example, reference to 'an excipient' is a reference to ***one or more*** excipients"—language absent from the '327 patent specification. *See Azurity*, 2021 WL 5332406, at *4. Moreover, the *Azurity* case's asserted patent did not include a "statistically significant" claim limitation. Ex. 25. Based on the claims and specification, the *Azurity* court found that "a buffer" in the claims was not limited to just one buffer. *Azurity*, 2021 WL 5332406, at *4. Here, Liquidia does not seek to limit "a"/"the" to the singular, and instead proposes the plain and ordinary meaning of these terms in view of the specification, which is very different from the

claims and specification at issue in the *Azurity* case.[9] Indeed, because the '327 patent requires "statistically significant" increases or reductions in treatment outcomes, departure from "a"/"the" meaning "one or more" is warranted. *See* '327 patent, cls. 2, 4, 6–7, 9.

UTC criticizes Liquidia for "attempt[ing] to nitpick the specification—not the claims[,]" but it is the claims, read in the context of the specification, that informs Liquidia's proposed construction. Reply, 14–15; Response, 10–11. And UTC's invalidity contention argument as an alleged admission by Liquidia is to no avail (*see* Reply, 15), because Liquidia never made such a concession. The fact that Liquidia made no other revision to its invalidity contentions, as UTC acknowledges, proves Liquidia's invalidity arguments have been consistent with its proposed construction presented here and the error was only typographical in nature. *See id.*

Finally, UTC argues that claim 2 of the '327 patent, which requires a "statistically significant" result "does not require a doctor to treat multiple patients and aggregate data from those patients for UTC to prove infringement of that claim." Reply, 15–16.[10] UTC is wrong and is contradicted by its own physician expert who testified that it is not possible to determine statistical significance within a single patient for a treatment. Ex. 19, 71:9–72:3. UTC cannot offer a construction that excludes treating a single PH-ILD patient to preserve the validity of certain claims, but later assert that treatment of a single PH-ILD patient would nonetheless infringe that same claim. Response, 11.

---

[9] The *Pacira Pharmaceuticals* case cited by UTC is similarly distinguishable because the asserted patent claims lacked statistical significance limitations. 2023 WL 3841559, at *12–13. UTC's citation to the general rule in *01 Communique Lab., Baldwin,* and *Abtox* are similarly unavailing because the claims and the specification here dictates departure from the general rule of those cases. *See* Reply, 12–14.

[10] Importantly, UTC does not contend that claims 4, 6-7, 9, all requiring a "statistically significant" result, can be infringed by treating a single patient.

B. "maximum tolerated dose" (claim 1)

Plaintiff's Proposed Construction	Defendant's Proposed Construction
Not indefinite. No construction necessary. To the extent the term is construed, it should be construed to have its plain and ordinary meaning in view of the specification, which is: "the highest dose that does not cause unacceptable adverse events"	Indefinite. If not indefinite, "the highest dose before a patient discontinues administration"
UTC understands that Liquidia may assert that this term is indefinite and its proposed construction appears to be a litigation-inspired attempt to support its indefiniteness argument.	The construction of "a maximum tolerated dose" is relevant to invalidity, particularly indefiniteness under § 112.

1. Plaintiff's Opening Position

The term "maximum tolerated dose" is definite and does not require construction. The term is known in the art and the intrinsic evidence is consistent with that known, plain and ordinary meaning. Indeed, the labels for other treprostinil products, including Tyvaso's—which instruct physicians and patients how to use the product—incorporate the same concept of tolerability. To the extent the Court finds construction necessary, however, it should be construed as "the highest dose that does not cause unacceptable adverse events."

Neither Liquidia's proposed construction nor its indefiniteness argument is tenable. Liquidia predicates its indefiniteness argument only upon alleged problems with UTC's *construction*, not the term itself. Ex. 1 (Invalidity Contentions) at 168-69. But Liquidia's reluctance to agree with UTC's construction does not change the fact that the POSA would understand what a maximum tolerated dose is. Moreover, the fact that Liquidia proposes a construction that it

presumably believes to be cogent undermines its position that this term is indefinite. Liquidia's construction is unsupported and should be rejected.

(i) The POSA would understand the plain and ordinary meaning of "maximum tolerated dose."

It is black-letter law that terms should be understood to have their plain and ordinary meaning to the POSA in view of the specification. *Phillips*, 415 F.3d at 1315 ("[T]he specification is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." (quotation marks omitted)). This is even more true when that specification defines its terms to have their plain and ordinary meaning. *See* Ex. B ('327 patent) at 7:11-14 ("Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this present technology belongs."). As explained more fully below, because the POSA is familiar with the meaning of "maximum tolerated dose," and that meaning is consistent with the intrinsic evidence, the term is not indefinite and does not need construction.

Claim 1 of the '327 patent describes "improving exercise capacity in a patient having [PH-ILD]" by administering "an effective amount of at least 15 micrograms up to a maximum tolerated dose of treprostinil . . . in a single administration event that comprises at least 6 micrograms per breath." Thus, the POSA would understand that the maximum tolerated dose is the highest ("maximum") quantity of inhaled treprostinil ("dose") that is "tolerated" in the context of treating a patient with PH-ILD to improve exercise capacity.

Liquidia appears to agree that "maximum" means "highest" and that "dose" does not need definition. The lone dispute, therefore, is what it means for a PH-ILD patient to "tolerate" a dose of inhaled treprostinil. UTC contends that the known, plain and ordinary meaning of tolerance in the context of the term "maximum tolerated dose" involves whether a patient can accept any

adverse events or side effects, and Liquidia contends that tolerance requires the patient to discontinue use—i.e., cease administration entirely. Only UTC's construction is consistent with the POSA's understanding.

The '327 specification explains that a "therapeutically effective amount can be determined by titrating the dose upwards from a starting dose, either in terms of dose by administration or frequency of administration." Ex. B ('327 patent) at 6:56-59. It further explains that a "therapeutically effective dose is determined by titrating the dose upwards until the *maximum tolerated dose* for the individual subject is determined." *Id.* at 6:59-62 (emphasis added). Consistent with that description, the specification describes a clinical trial in which "[i]nvestigators adjusted the dose on an individual patient basis to achieve the *maximum tolerated dose* leading to functional improvement." *Id.* at 29:51-54 (emphasis added). The patent also discloses the assessment of adverse events, including frequency, extent, and type (*id.* at Table 6, Table 9, 35:15-24, 51:35-40), and describes tolerability in the context of adverse effects experienced by patients, explaining that "[t]ransition from Tyvaso to TreT was safe and well tolerated" because "[m]ost adverse effects (AEs) were mild to moderate in severity." *Id.* at 51:35-37 (discussing Example 5). Thus, the patent uses "maximum tolerated dose" to refer to a dose determined by an individual patient's ability to tolerate the medication and any resulting adverse effects, while experiencing clinical benefit. *Id.* at 6:40-7:3, 29:40-55; 51:35-37.

References incorporated into the '327 patent provide additional examples of titration to determine an individual's maximum tolerated dose—further demonstrating that the POSA would understand what tolerance means—including (1) Sorbera, a 2001 publication regarding treprostinil, which describes a clinical study that determined "individual maximum tolerated doses" of Remodulin® in view of "[d]ose limiting adverse events," and (2) U.S. Patent No.

8,765,813, which describes titrating a patient's treprostinil dose upward "by 1 ng/kg/min every 7 days until the patient reached his maximum tolerated dose," after which the patient was "unable to tolerate higher doses due to diarrhea and jaw pain, commonly reported dose limiting side effects of prostacyclin therapy." D.I. 94 (JCCC Ex. C) (Sorbera) at 150-151; Ex. C ('813 patent) at 184-186 (12:40-49).

Titrating doses upward to the maximum tolerated dose was well known in the PH field well before the '327 patent. Indeed, the 2009 Tyvaso label, which is cited on the face of the '327 patent (Ex. B ('327 patent) at 7), directs physicians to start with a dose of inhaled treprostinil using 3 breaths (18 micrograms), and to reduce that dose "[i]f 3 breaths are not *tolerated*." Ex. 3 (2009 Tyvaso Label) at 1 (emphasis added). By definition, reducing the dose means continuing the administration at a lower level, not discontinuing it entirely. Likewise, the dose should be increased each 1-2 weeks, "if *tolerated*." *Id.* (emphasis added). Overall, the treatment described in the label requires "[t]itrat[ing] to target maintenance dosage . . . as *tolerated*." *Id.* (emphasis added). The 2004 label for Remodulin (intravenous or subcutaneous treprostinil) also describes adjusting the dose according to tolerance, stating that the "goal of chronic dosage adjustments is to establish a dose at which PAH symptoms are improved, while minimizing excessive pharmacologic effects of Remodulin (headache, nausea, emesis, restlessness, anxiety and infusion site pain or reaction)." Ex. 4 (2004 Remodulin Label) at LIQ_PH-ILD_00018730; *see also id.* ("If this initial dose cannot be tolerated because of systemic effects, the infusion rate should be reduced . . . ."). This reflects PH clinical practice, in which a physician may direct a patient to increase the dose until the disadvantages of that treatment (adverse effects) outweigh the benefits. It does not state or imply that, if a patient experiences adverse effects at a particular dose, the patient should stop all administration entirely.

The file history further confirms that "maximum tolerated dose" was known and does not need construction. In response to anticipation rejections, UTC amended claim 1 to recite "maximum tolerated dose." Ex. C ('327 Patent File History, Office Action Response) at 130-37. Following UTC's response, the examiner withdrew his rejections—without asking what a maximum tolerated dose was or issuing § 112 rejections—and allowed the application. *Id.* ('327 Patent File History, Notice of Allowance) at 138-43.

Liquidia's own documents also show that, at least when it is speaking to the public instead of trying to conjure an invalidity defense in litigation, it understands what tolerance means. In its corporate overview and regulatory submissions, Liquidia has stated that the "[g]oal of prostanoid therapy is to dose to [the] highest *tolerable* level to provide symptomatic benefit." Ex. 5 (Liquidia Corp. Overview) at LIQ_PH-ILD_00000543 (emphasis added); Ex. 6 (Liquidia 2018 Form 10-K) at UTC_PH-ILD_003175 ("The goal of treatment targeting the prostacyclin pathway is to maximize a patient's exposure to the highest tolerable level of drug."); Ex. 7 (Liquidia 2019 Form 10-K) at UTC_PH-ILD_003398 (same). Liquidia's own proposed product label describes increasing the dose each week, "as tolerated." Ex. 8 (Yutrepia™ Label) at LIQ_PH-ILD_00000898.

The term "maximum tolerated dose" is known, understood, and does not need construction. Nevertheless, to the extent the Court is inclined to construe the term, the evidence above establishes that the POSA would understand the plain and ordinary meaning of "maximum tolerated dose" based on the claim language, the specification, the prosecution history, and the term's meaning in the art, to mean "the highest dose that does not cause unacceptable adverse events." *See supra* § VI.B.1, at 19-22.

(ii) Liquidia's proposed construction is not supported by the intrinsic evidence.

Liquidia's proposed construction—"the highest dose before a patient discontinues administration"—undermines its indefiniteness position and lacks support. There is nothing in the claims, specification, or prosecution history equating "tolerance" with *discontinuing* administration, including the portions Liquidia cited in the Joint Claim Construction Chart. Ex. A (JCCC) at 6-7. Liquidia's citations mention or relate to subjects discontinuing from example clinical studies. *Id.*; Ex. B ('327 patent) at 4:30-41, 6:1-4, 32:20-27, Fig. 2, Fig. 12, Table 12. But none of these passages demonstrate lexicography involving "discontinuation." Indeed, Liquidia has asserted that "the '327 patent does *not* explicitly define 'maximum tolerated dose.'" Ex. 1 (Invalidity Contentions) at 168 (emphasis added). Nor does Liquidia explain why these passages would somehow override the plain and ordinary meaning known to the POSA and even used by Liquidia itself in its public filings. *See supra* § VI.B.1, at 19-22. There is no indication that any of the disclosed patient discontinuations were related to the treprostinil dose at discontinuation. In fact, Liquidia cites Example 3, which describes 38 patients in the placebo arm prematurely discontinuing treatment compared to 40 patients in the treprostinil arm. Ex. B ('327 patent) at 4:30-41, 32:20-27, Fig. 2. But Figure 2 (the plan for Example 3) describes discontinuations for reasons other than treprostinil dose, including protocol violations, withdrawals, and "other reason[s]." Thus, there is no basis to conclude that discontinuation from the disclosed trial has any relevance to or bearing on "maximum tolerated dose."

(iii) "Maximum tolerated dose" is not indefinite.

Liquidia bears the burden of showing, by clear and convincing evidence, that "maximum tolerated dose" is so unclear that the POSA would not understand the term with reasonably certainty. *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 901 (2014); *BASF Corp. v.*

Johnson Matthey Inc., 875 F.3d 1360, 1365 (Fed. Cir. 2017). Liquidia cannot meet this high hurdle. The words are clear, and the POSA, the USPTO examiner, and the parties all understand the term.

As noted above, the examiner necessarily considered "maximum tolerated dose," understood its meaning, and was able to apply the scope and meaning of the claim term to the prior art, demonstrating that the term is not indefinite. *See supra* § VI.B.1, at 22; *Sonix Tech. Co., Ltd. v. Publ'ns Int'l, Ltd.*, 844 F.3d 1370, 1379-80 (Fed. Cir. 2017) ("Although . . . application by the examiner and an expert do not, on their own, establish an objective standard, they nevertheless provide evidence that a skilled artisan did understand the scope of this invention with reasonable certainty.").

Indeed, Liquidia itself has had no problem interpreting "maximum tolerated dose." Instead of asserting indefiniteness during the preliminary injunction proceedings, Liquidia's counsel was able to compare the doses claimed in the '793 patent with those claimed in the '327 patent and, in turn, argue that they are the same. Ex. 9 (PI Hearing Tr.) at 44:21-22 (Liquidia's counsel: "With respect to dosing, UTC argued today that the dosing is different. It's not.").

Lacking any genuine evidence for indefiniteness, Liquidia's Invalidity Contentions instead frame its indefiniteness position entirely upon UTC's proposed construction. *See* Ex. 1 (Invalidity Contentions) at 168-69 ("Thus, under UTC's proposed construction of 'maximum tolerated dose,' a POSA would not have reasonable certainty as to the precise scope of Asserted Claim 1, rendering it indefinite."). As explained above, "maximum tolerated dose" does not even need construction. Moreover, Liquidia's attorney argument about UTC's proposed construction cannot meet Liquidia's clear and convincing burden. *See Sonrai Memory Ltd. v. Kingston Tech. Co., Inc.*, 2022 WL 3640302, at *5 (W.D. Tex. Aug. 23, 2022) (finding "[d]efendants' argument that the term is indefinite is undercut by [d]efendants' proposed construction, which indicates that a POSITA

would understand the meaning of this claim term with reasonable certainty"). The Court should reject Liquidia's indefiniteness argument and unsupported construction and either decline to construe the term or adopt UTC's proposed construction.

2. Defendant's Answering Position

(i) "maximum tolerated dose" is indefinite

Patent claims are indefinite when, "read in light of the specification . . . fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention." *Nautilus*, 572 U.S. at 901. The Federal Circuit has found claims indefinite when there are different methods to calculate a claimed parameter, the specification does not teach which method to use, and each method results in materially different claim scope. *See, e.g.*, *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 789 F.3d 1335, 1345 (Fed. Cir. 2015) (finding the term "molecular weight" was indefinite because it could be measured using three methods, the specification did not teach which method to use, and each method yielded different results); *see also Dow Chem. Co. v. Nova Chems. Corp. (Canada)*, 803 F.3d 620, 634 (Fed. Cir. 2015) (finding the challenged claims were indefinite where there were multiple ways of measuring a claimed parameter that led to different results and the specification and prosecution history provided no guidance). Here, the claim term "maximum tolerated dose" is indefinite because the specification and claims of the '327 patent disclose multiple outcome measures for determining when a patient has reached a "maximum tolerated dose" each yielding a different "dose," without any guidance as to which outcome should be followed when interpreting the claims.

First, the asserted claims identify a different outcome to measure during the method of treating PH-ILD. In particular, independent claim 1 recites a "method of improving exercise capacity in a patient having [PH-ILD] . . . comprising administering . . . an effective amount of . . . up to a maximum tolerated dose of treprostinil[,]" ('327 patent, 54:6–14 (claim 1)), and claim 5

(which depends on claim 1) claims a reduction in NT-proBNP levels "by at least 200pg/mL" (*id.* at 54:27–30 (claim 5)). The '327 patent's specification, however, makes clear that the "maximum tolerated dose" differs depending on the particular outcome measured. Table 5 shows the results of the INCREASE clinical trial, which compared inhaled treprostinil with placebo. *See id.* at Table 5. While all patients treated with treprostinil demonstrated an "improv[ed] exercise capacity" (as measured by an increase in six-minute walk distance ("6MWD") (Table 5 at col. 32, "Primary end point"), Table 5 also makes clear that the observed range of NT-proBNP levels showed an increase of up to 5,373.1 pg/ml (*id.*, "Secondary end points"). Because the patients described in Table 5 received the same dose of treprostinil, Table 5 demonstrates that a "maximum tolerated dose" leads to an "improv[ed] exercise capacity" as required by claim 1, but not necessarily to a reduction in NT-proBNP levels, as required by claim 5. In this circumstance—as dictated by the claims—if a patient's 6MWD improves but their NT-proBNP levels increase, it is uncertain whether that patient reached the "maximum tolerated dose." The specification and claims provide no guidance on how to reconcile the contradictory outcomes described in Table 5 and, thus, fail to provide a POSA with any reasonable certainty as to whether a patient has reached the "maximum tolerated dose."

Second, the '327 patent does not define "maximum tolerated dose." It, instead, uses this term only twice in the entire specification. The first instance of "maximum tolerated dose" appears in the statement "the therapeutically effective dose is determined by titrating the dose upwards until the ***maximum tolerated dose*** for the individual subject is determined." '327 patent, 6:59– 62 (emphasis added). According to the '327 patent, a dose is "therapeutically effective" if it "effect[s] treatment," which in turn requires delaying disease onset, disease symptoms, and disease progression. *See id.* at 6:47–52, 6:63–7:3. Taken together, this portion of the '327 patent teaches a POSA that, if a patient's disease is not yet delayed, not yet inhibited, or is progressing, the patient

has not yet reached the "maximum tolerated dose." However, when a patient's disease begins progressing, the '327 patent teaches all treatment should be discontinued. As seen in Figure 2, several patients enrolled in the INCREASE clinical trial discontinued treatment once their disease had progressed. *See id.* at Figure 2 (showing that six patients in the treatment group discontinued prematurely and four patients discontinued study participation due to progressive disease). These portions of the '327 patent teach a POSA to discontinue treatment once the "maximum tolerated dose" has been reached and the patient's disease begins progressing.

The second instance of "maximum tolerated dose" appears in column 29 of the '327 patent: "Investigators adjusted the dose on an individual patient basis to achieve the ***maximum tolerated dose*** leading to functional improvement." *Id.* at 29:51–54 (emphasis added). Although the '327 patent does not define "functional improvement," it is clear that a change in 6MWD would be considered a functional improvement, given that the 6MWD was the primary endpoint of the INCREASE study. *Id.* at 30:44–52 (explaining that the INCREASE study's primary clinical endpoint measured change in peak 6MWD). Moreover, there is no indication in the '327 patent whether "functional improvement" is co-extensive with "therapeutically effective dose," appearing in the first instance of "maximum tolerated dose." Nonetheless, as shown in Table 5, patients did achieve a functional improvement in the 6MWD test. *Id.* at Table 5. But looking at the '327 patent as a whole, it is unclear whether a "maximum tolerated dose" was achieved if the patient experienced a "functional improvement," yet did not achieve another claimed outcome measure, like NT-proBNP, or had to discontinue treatment.

Further compounding the uncertainty associated with "maximum tolerated dose" is Table 6 of the '327 patent. Table 6 shows the number of adverse events that occurred during the INCREASE study. *See id.* at Table 6. Table 6 demonstrates that 93.3% of patients that received

inhaled treprostinil experienced an adverse event. *See id.* at Table 5, col. 58. Notably, Table 6 shows that 47 patients in the treatment group withdrew from the INCREASE study due to adverse events. *See id.* If a patient's exercise capacity improves (as measured by an increase in the 6MWD as demonstrated by Table 5, or any of the claimed outcome measures are reduced or improved as claimed[11]), but treatment is withdrawn due to the adverse events, there is no reasonable certainty as to whether that patient is deemed to have reached the "maximum tolerated dose." And the specification does not parse out the positive outcome demonstrated in Table 5 from the adverse events from Table 6 and Figure 2. The ambiguity in the '327 patent provides further evidence that a "maximum tolerated dose" is indefinite.

The indefiniteness of "maximum tolerated dose" is underscored by UTC's proposed construction of the term, which merely defines the indefinite phrase "maximum tolerated dose" with another indefinite phrase "unacceptable adverse events." *See* Opening Br., 18. As noted above, almost all patients that received treprostinil experienced an adverse event. The specification provides no description as to which of those adverse events are acceptable and which are unacceptable. Thus, even UTC is unable to provide reasonable certainty as to what is and is not a "maximum tolerated dose."

As is clear from the specification, determining what constitutes a "maximum tolerated dose" depends on which outcome, as claimed and disclosed in the specification, a POSA measures.

[11] The asserted claims each identify a different outcome to measure during the method of treating PH-ILD. For instance, claims 1, 2, 3 and 17–19 assess improvement in "exercise capacity" and in particular outcomes based on the six-minute walk distance test. '327 patent at 54:6–22 (claims 1–3); *id.* at 55:1–9 (claims 17–19). Claims 4 and 5 look at a different outcome measure, reduction in plasma concentration of NT-proBNP (*see id.* at 54:23–30 (claims 4–5)), whereas claims 6 and 7 assess different outcome measures including "reduction of at least one exacerbations of the interstitial lung disease" (*id.* at 54:31–33 (claim 6)), and "reduction of clinical worsening events due to the interstitial lung disease" (*id.* at 54:31–36 (claim 7)). And asserted claims 9-10 assess yet another outcome measure, forced vital capacity. *Id.* at 54:42–49 (claims 9–10).

And the '327 patent's specification also makes clear that confounding outcomes can be achieved with the same dose. Moreover, the '327 patent specification provides different responses once a "maximum tolerated dose" is achieved including continuing treatment and discontinuing treatment. *Compare* '327 patent at Figure 2 (showing discontinuation upon disease progression) *with id.* at 29:51–54 (explaining that the dose should be adjusted once a patient reaches the "maximum tolerated dose"). Because the '327 patent does not indicate which of the many outcomes should take priority when determining the "maximum tolerated dose," and because different doses might be needed to achieve the various claimed outcomes, the specification does not provide "clear notice of what is claimed, thereby appris[ing] the public of what is still open to them[,]" and thus, the Court should find "maximum tolerated dose" indefinite. *Nautilus*, 572 U.S. at 909 (internal quotation marks omitted) (citation omitted).

(ii) To the extent "maximum tolerated dose" is not indefinite, it should be construed as "the highest dose before a patient discontinues administration"

To the extent the Court finds the term "maximum tolerated dose" is not indefinite, Liquidia proposes the following construction: "the highest dose before a patient discontinues administration." For example, Table 6 of the '327 patent shows that out of the 890 adverse events that occurred in the treatment arm of the INCREASE study, 47 led to withdrawal from the study. *See* '327 patent at Table 6; *see also id.* at Table 18 (showing that certain adverse events led to patient withdrawal from the TRIUMPH clinical study).[12] Figure 2 of the '327 patent further demonstrates that patients who experienced disease progression discontinued treatment. *See id.* at Figure 2 (showing that patients in the treatment group discontinued study participation due to progressive disease). These teachings support Liquidia's proposed construction and avoid the

[12] "AEs" as used in Table 18 refers to adverse events.

ambiguity infused into the claims by UTC's proposed construction of "maximum tolerated dose." Accordingly, to the extent the Court determines that the phrase "maximum tolerated dose" is definite, then Liquidia respectfully requests the Court adopt Liquidia's proposed construction as it would provide certainty as to whether the "maximum tolerated dose" was achieved.

(iii) UTC's reliance on intrinsic and extrinsic evidence does not render "maximum tolerated dose" definite

UTC asserts that the term "maximum tolerated dose" is not indefinite. Opening Br., 18, 23–25. UTC's arguments, however, ignore the specification and moreover, misapply the prosecution history and extrinsic evidence. First, UTC's analysis of the specification overlooks the inherent contradiction between the claims and the specification discussed *supra*—particularly claims 1, 5, and 7 and Tables 5 and 6. UTC does not, and cannot, reconcile the conflicting data presented in the '327 patent as to what dose may be considered the "maximum tolerated dose." For that reason alone, the Court should find that "maximum tolerated dose" is indefinite.

Second, UTC's reliance on the '327 patent's file history to argue in favor of definiteness is misplaced. According to UTC, the patent examiner's failure to reject claim 1 after the applicant amended it to recite "maximum tolerated dose" allegedly demonstrates that a POSA knew the plain and ordinary meaning of this term. *See* Opening Br., 22. Here, there is no evidence of how the examiner or the inventor understood the term "maximum tolerated dose." Simply because the examiner did not issue a claim rejection based on the term "maximum tolerated dose" does not mean the term is definite. Such a rule would lead to the absurd result that all claim terms are definite if the patent examiner never raised an issue or rejection based on that term during prosecution.

Third, UTC's reliance on Liquidia's documents (extrinsic evidence) fares no better. To begin with, Liquidia's statements bare no relevance to the meaning of the phrase "maximum tolerated dose" in UTC's patent. Nonetheless, according to UTC, Liquidia's use of the word

"tolerate" (and its variants) in various corporate and regulatory documents demonstrates that the term "maximum tolerated dose" in the '327 patent is definite and should be construed as the highest level of drug a patient can tolerate. *See* Opening Br., 22. But "extrinsic evidence . . . may not be used to vary or contradict the claim language . . . [or] other parts of the specification." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1584 (Fed. Cir. 1996) (internal citation omitted). As discussed *supra*, Table 6 of the '327 patent demonstrates that a patient could reach the "maximum tolerated dose" even after experiencing adverse events that are intolerable enough to cause withdrawal of the treatment altogether. *Compare* '327 patent at Table 5 (showing that all patients in the treatment group experienced an increase in 6MWD) *with id.* at Table 6 (showing that 47 patients in the treatment withdrew treatment due to adverse events). The Court should, thus, not rely on the extrinsic evidence on which UTC relies because it contradicts the intrinsic evidence.

(iv) The intrinsic evidence does not support UTC's proposed construction of "maximum tolerated dose"

UTC argues that the term "maximum tolerated dose" does not require construction, but to the extent it does, UTC proposes construing the phrase to mean: "the highest dose that does not cause unacceptable adverse events." Opening Br., 18-25. As discussed above, because of the different outcomes associated with the "maximum tolerated dose" phrase, to the extent it is not indefinite, the Court should adopt Liquidia's proposed construction. Further, the Court should reject UTC's proposed construction because its construction is indefinite for the reasons provided above and separately, the '327 patent does not disclose instances where administration of treprostinil "does not cause" adverse events, let alone what is considered an "unacceptable adverse event."

The '327 patent explains that there were a total of 890 reported adverse events for the 163 patients enrolled in the treatment arm, 53 serious adverse events, and 47 adverse events leading to

withdrawal from the study. *See* '327 patent at Table 6. Table 6 further discloses that 93.3% of patients in the treatment arm of the INCREASE study experienced more than one adverse event, and 23.3% of patients experienced more than one "serious" adverse event. *See id.* at Table 6. As such, the treatment regimen disclosed and claimed in the '327 patent did cause "adverse events" and there is no indication that any single patient did not experience some type of adverse event, let alone at a "maximum tolerated dose" as UTC's construction requires.

Because adverse events did occur, UTC's proposed construction would require a POSA to determine the "maximum tolerated dose" that may cause an adverse event, but that is *not* deemed "unacceptable." Here again, the specification fails to support this construction as there is no guidance provided as to what would be considered an "acceptable" adverse event as compared to an "unacceptable" adverse event, let alone at what "maximum tolerated dose" that would occur. To be clear, the '327 patent does not indicate whether any adverse event is unacceptable, some adverse events are acceptable and others are not, or whether only "serious" adverse events are unacceptable. And to the extent UTC contends each doctor and patient can make the assessment as to whether an adverse event is acceptable or not at the time of administration, UTC's construction would then necessarily rely on extrinsic evidence, as opposed to intrinsic evidence.[13]

Because the intrinsic evidence offers no support for UTC's proposed construction and the extrinsic evidence UTC cites has no bearing on the parties' dispute, the Court should reject UTC's proposed construction.

[13] UTC's argument also leads to a finding on non-infringement, as the proposed Yutrepia® label as it pertains to the PH-ILD indication, does not instruct doctors or patients to assess whether an adverse event is acceptable or "unacceptable." *See* Ex. 8 at § 2 "Dosage and Administration", § 14.2 "Pulmonary Hypertension Associated with ILD (WHO Group 3)".

3. Plaintiff's Reply Position

Liquidia's attempt to invalidate every claim of the '327 patent by construing "maximum tolerated dose" as indefinite—purely through attorney argument—fails. Each and every claim of the patent is presumed valid. Typically, parties asserting that POSAs cannot understand the meaning of a phrase engage experts in the field to identify and explain the POSA's confusion. Liquidia failed to do so here—apparently unable to find an expert willing to claim they did not know what "maximum tolerated dose" is. Liquidia sets forth no *evidence* that the POSA would not understand the '327 patent's claims with reasonable certainty.

(i) The claims of the '327 patent are not indefinite.

The POSA would understand the term "maximum tolerated dose" with reasonable certainty and Liquidia presents no evidence to the contrary.

First, Liquidia incorrectly suggests that the claims of the '327 patent are indefinite because there are allegedly different "outcome measures" and "different methods to calculate" a maximum tolerated dose, but Liquidia never explains what those "different methods" are in the context of the '327 patent's claims. *Supra* § VI.B.2, at 25-26. Liquidia also has no support for its bald assertion that the POSA would understand the patent to require different "outcome measures" that *limit* maximum tolerated dose such that "each yield[s] a different 'dose.'" *Supra* § VI.B.2, at 25.

Liquidia's premise is flawed. Unlike *Teva,* where "molecular weight" could be measured using three distinct, well-defined techniques (789 F.3d at 1341-45), or *Dow,* where "there were multiple ways of measuring a claimed parameter that led to different results" (803 F.3d at 631-35), Liquidia provides no evidence that the '327 patent provides different methods of measuring "maximum tolerated dose," much less methods that *require* "different results." The '327 patent exposes the flaws in Liquidia's argument. For example, claim 1 recites "15 micrograms up to a maximum tolerated dose," and the dependent claims add limitations narrowing the scope of claim

1. Ex. B ('327 patent) at claims 1-11 and 14-19. Liquidia provides no evidence or expert testimony that the POSA would understand that these additional limitations increase or decrease—let alone redefine—"maximum tolerated dose" that is recited in claim 1. Absent this evidence, Liquidia's argument crumbles.

Liquidia's "contradictory outcomes" argument is similarly flawed. *Supra* § VI.B.2, at 25-29. Liquidia posits, without support from an expert declaration, that a "maximum tolerated dose" was achieved in Table 5 of the '327 patent sufficient to "improve exercise capacity . . . but not necessarily . . . a reduction in NT-proBNP levels, as required by claim 5." *Id.* at 26. The data in Table 5 are not "contradictory." Nor is it "contradictory" for claims 1 and 5 or any of the asserted claims to differ in scope. Liquidia seems to argue that a single patient must always simultaneously fall within the scope of dependent claim 5 if it falls within the scope of independent claim 1—but that is legally and factually flawed, as no such requirement exists.

Second, Liquidia argues that "maximum tolerated dose" is indefinite because it must be "taken together" with the term "therapeutically effective dose . . . which in turn requires delaying disease onset, disease symptoms, and disease progression." *Supra* § VI.B.2, at 26-27. This piggy-backing of limitations imported from the specification is misguided. At bottom, Liquidia's position is that "the '327 patent teach[es] a POSA to *discontinue* treatment once the 'maximum tolerated dose' has been reached and the patient's disease begins progressing." *Id.* (emphasis added). There is no evidence that the POSA would understand "maximum *tolerated* dose" only via complete "discontinuation."

The inventors did not claim a method of treatment based on *discontinuation* of treatment. Under Liquidia's view, "maximum tolerated dose" is only known *after* a patient discontinues use. But the specification describes in some embodiments "titrat[ing] upward, as clinically tolerated,

to identify a maximum stable dose in each subject." Ex. B ('327 patent) at 6:1-4. The specification is consistent both with claim 1, which includes dosing from "15 micrograms *up to* a maximum tolerated dose of treprostinil" (emphasis added), and the existing clinical standard of care for treprostinil. *Supra* § VI.B.1, at 19-22.

Liquidia argues that Tables 5 and 6 inject "ambiguity" into the meaning of "maximum tolerated dose." *Supra* § VI.B.2, at 25-29. Not so. Liquidia—again without the support of any expert testimony—mischaracterizes these tables and erroneously asserts that all volunteers received the same treprostinil regimen to argue that the claimed methods' outcomes require "reach[ing]" the maximum tolerated dose and that this requirement purportedly leads to contradictory outcomes. *Id.* First, neither Table 5 nor 6 discuss "maximum tolerated dose" whatsoever. Consequently, any argument purporting to link Tables 5 and 6 to "maximum tolerated dose" is speculative and tenuous at best. Liquidia erroneously uses volunteer withdrawal as a proxy for "maximum tolerated dose." But Table 6 discloses withdrawals totaling 47 and 38 for the treprostinil and placebo arms of the study, respectively. Obviously, patients receiving the placebo were not administered a maximum tolerated dose of treprostinil.

A patient's ability to tolerate a medication (i.e., his/her "maximum tolerated dose") is simply not the same as clinical efficacy, and Liquidia has provided no evidence to suggest otherwise. While different dependent limitations may be achieved with different "effective amounts" of treprostinil, Liquidia presents no evidence that the *tolerability* of treprostinil in a patient will "depend on which outcome . . . a POSA measures." That is because the claimed administration is patient-specific and requires administering an "effective amount" in each subject.

(ii) "Maximum tolerated dose" need not be construed; but if construed, UTC's proposed construction should be adopted.

Liquidia never explains why the POSA would not understand "maximum tolerated dose" with reasonable certainty. Because this is the threshold question for indefiniteness, the Court need not construe the term at all. To the extent the Court believes "maximum tolerated dose" needs further clarification, UTC's construction is fully supported by the specification.

The '327 patent teaches the POSA that dosing is dependent on "safety and tolerability." *E.g.*, Ex. B ('327 patent) at 22:30-37, 47:34-39. And the "safety profile of inhaled treprostinil observed in this vulnerable patient population" was known to the POSA because it was "similar to that reported in previous studies." *Id.* at 35:49-51. The POSA would also understand that "[t]he most frequently reported adverse events were cough, headache, dyspnea, dizziness, nausea, fatigue, and diarrhea." *Id.* at 35:51-53. Based on this data, the patent teaches the POSA that the claimed methods of treatment are both safe and well tolerated.

Despite this, Liquidia argues without evidence that "UTC's proposed construction" is also "indefinite." *Supra* § VI.B.2, at 28-29, 31. Liquidia attempts to flip the burden of proof by arguing that "UTC is unable to provide reasonable certainty[.]" *Id.* at 28-29. But it is always Liquidia's burden to prove indefiniteness by clear and convincing evidence. *BASF Corp.*, 875 F.3d at 1365.

Liquidia also complains that "the '327 patent does not disclose instances where administration of treprostinil 'does not cause' adverse events." *Supra* § VI.B.2, at 31. This is a red herring. UTC's proposed construction is "the highest tolerated dose that does not cause unacceptable adverse events," which makes clear that some adverse events are permissible. Liquidia complains that "the assessment as to whether an adverse event is acceptable or not at the time of administration" would "necessarily rely on extrinsic evidence." *Id.* at 32. But again, Liquidia fails to present *any* evidence that the POSA would not understand how to determine a

"maximum tolerated dose" when the "safety profile of inhaled treprostinil observed in this vulnerable patient population" was known in the art because it was "similar to that reported in previous studies." Ex. B ('327 patent) at 35:49-51.

4. Defendant's Sur-Reply Position

(i) "Maximum tolerated dose" is indefinite

UTC contends that this term is not indefinite because a POSA would understand its meaning. But to make this argument, UTC ignores the different outcome measures in the claims, the different uses of the term in the specification, and the different outcomes presented in the disclosed Tables—the very context which demonstrates the term is indefinite. UTC's reply only reinforces that this term is indefinite. Reply, 33–35.

UTC argues this case is unlike *Teva* because "Liquidia provides no evidence that the '327 patent provides different methods of measuring . . . ." Reply, 33. UTC, however, ignores its own claims. Response, 25–26. The claims provide several different outcome measures—including increased exercise capacity (claims 1–3), reduction in NT-proBNP levels (claims 4–5), reduction in clinical worsening (claims 6–8), and improvement of FVC (claims 9–10)—all requiring a "maximum tolerated dose." *See* Response, 25–26; '327 patent, cls. 1–10. As in *Teva*, the '327 patent's specification does not teach which outcome to use in order to determine whether the "maximum tolerated dose" has been achieved, and each measured outcome can be achieved with a different maximum tolerated dose, thereby rendering the claim term indefinite. *See Teva*, 789 F.3d at 1345; *see also* Response, 25.

UTC also relies on claim 1's recitation of a minimum dose ("at least 15 micrograms") and a "maximum tolerated dose," and asserts that "the dependent claims add limitations narrowing the scope of claim 1." Reply, 33–34. But these do nothing to inform a POSA what the "maximum tolerated dose" would be. And none of the dependent claims "narrow" the scope of the doses

recited in claim 1. Instead, they add additional outcome measures that *must* be met in addition to the improvement in exercise capacity recited in claim 1, with no indication or guidance as to which "maximum tolerated dose" is required for each different outcome measure.[14]

Further, Liquidia is not, as UTC contends, "piggy-backing" a specification limitation, but instead using the specification as it is meant to be used: to exemplify how "maximum tolerated dose" is used, because it is not otherwise defined. *See* Reply, 34. Liquidia identified two instances in the '327 patent's specification that mentioned "maximum tolerated dose"—once in the context of "therapeutically effective dose" and another in the context of "functional improvement."[15] *See* Response, 26–29. The former described determining a "maximum tolerated dose" in terms of discontinuing treatment and the latter described it in terms of functional improvement. *Id.* Because the specification provides two competing outcomes for whether a patient has reached the "maximum tolerated dose," and no guidance as to which outcome should take precedent, "maximum tolerated dose" is indefinite. *Id.* Indeed, UTC admits as much stating no POSA "would understand 'maximum tolerated dose' **only** via complete 'discontinuation.'" Reply, 34 (emphasis added).

UTC next argues Tables 5 and 6 do not inject any ambiguity into the term "maximum tolerated dose." *Id.* at 35. UTC's arguments fall flat. That Tables 5 and 6 do not mention the phrase "maximum tolerated dose" does not make them "speculative and tenuous" to the meaning of the

[14] UTC erroneously asserts that Liquidia argues "a single patient must always simultaneously fall within the scope of dependent claim 5 if it falls within the scope of independent claim 1[.]" Reply, 34. As Liquidia argued, because claim 5 depends from claim 1, a single patient must meet the limitations of claim 1 if they are also to meet the limitations of dependent claim 5. Response, 25–26.

[15] UTC does not address the use of "maximum tolerated dose" in conjunction with functional improvement, which is not surprising, as it further emphasizes the lack of reasonable certainty associated with the phrase. Reply, 33–35.

disputed phrase because they summarize the clinical endpoints and patient withdrawals based on the dosing in the INCREASE study. Table 5 assesses many of the clinical endpoints UTC now claims are directly implicated in determining whether a patient has reached the "maximum tolerated dose." *See* '327 patent, Table 5. And, whether individuals in the placebo group from Table 6 withdrew has no bearing on the "maximum tolerated dose," because those individuals never received any dose of treprostinil. 163 patients in Table 6 did receive treprostinil, and that was what Liquidia pointed to in its briefing. Response, 31–32. Based on the claim language and specification, "maximum tolerated dose" is indefinite.

(ii) Expert testimony is not required to find indefiniteness

Contrary to UTC's arguments (Reply, 33), it is not necessary to have expert testimony on the issue of indefiniteness. *See Teva*, 789 F.3d at 1342 ("A party cannot transform into a factual matter the internal coherence and context assessment of the patent simply by having an expert offer an opinion on it. The internal coherence and context assessment of the patent, and whether it conveys claim meaning with reasonable certainty, are questions of law."); *see also Dow*, 803 F.3d at 634 (finding that "the patent record—the claims, specification, and prosecution history" were sufficient "to ascertain if they convey to one of skill in the art with reasonable certainty the scope of the invention claimed"). The lack of expert testimony on indefiniteness should not prevent the Court from finding "maximum tolerated dose" indefinite.

(iii) UTC's construction adds ambiguity

UTC argues the '327 patent describes the "maximum tolerated dose" as depending on the "safety and tolerability" of treprostinil. *See* Reply, 36–37 (citing '327 patent, 22:30–37, 47:34–39). Based on the most frequently reported adverse events described in the '327 patent, UTC contends that a POSA would know that the claimed methods were "safe and well tolerated." This argument is a non-sequitur.

The portions of the '327 patent UTC cites do not link "maximum tolerated dose" to "safety and tolerability." *See, e.g.*, '327 patent, 22:30–37 (discussing final study visit assessments of adverse events and drug tolerance—not "maximum tolerated dose," as claimed); *see also id.* at 47:34–39 (discussing evaluation of safety and tolerability of treprostinil in patients with pulmonary arterial hypertension—not pulmonary hypertension associated with interstitial lung disease, as claimed—without any mention of dosing). Instead, the '327 patent associates the "maximum tolerated dose" with clinical outcomes, which supports Liquidia's position. *See id.* at 22:19–27 ("Study drug doses were maximized throughout the study. Dose escalations … could occur ... as clinically tolerated.").

UTC characterizes Liquidia's point that the '327 patent never discloses instances where treprostinil administration did not cause adverse events as a "red herring." Reply, 36–37. Whether adverse events are possible, however, is not responsive to Liquidia's contention that the '327 patent fails to teach what qualifies as an "unacceptable adverse event," as required by UTC's proposed construction. As a result, UTC's requirement to assess "unacceptable adverse events"—a term that never appears in the '327 patent's specification—injects further uncertainty into the asserted claims. In contrast, to the extent "maximum tolerated dose" is not indefinite, Liquidia's proposed construction avoids this ambiguity by focusing on discontinuation of treatment.

C. "pulsed inhalation device" (claims 11, 14)

Plaintiff's Proposed Construction	**Defendant's Proposed Construction**
"A device that provides for non-continuous inhaled drug delivery"	"A device that provides the force for non-continuous inhaled drug delivery"
UTC understands that Liquidia contends that it does not infringe claims 11 or 14 because Liquidia's dry powder inhaler is allegedly not a "pulsed inhalation device." Liquidia	The construction of "pulsed inhalation device" relates to non-infringement as Liquidia's device does not provide the force for non-continuous inhaled drug delivery.

Plaintiff's Proposed Construction	Defendant's Proposed Construction
contends that construction of this term makes a difference because it impacts Liquidia's infringement of claims 11 and 14.	

1. Plaintiff's Opening Position

The claimed "pulsed inhalation device" should be construed as "a device that provides for non-continuous inhaled drug delivery," which is consistent with the claims, specification, and other intrinsic evidence. Liquidia agrees that the "pulsed inhalation device" is a device that provides for non-continuous (*i.e.*, "pulsed") drug delivery by inhalation. But in an attempt to create a non-infringement position for claims 11 and 14, Liquidia also adds a limitation—based on extrinsic evidence only—requiring that the pulsed inhalation device itself must provide "***the force for***" the non-continuous inhaled delivery.

This added limitation, however, conflicts with the '327 patent specification and would exclude example embodiments the inventors identified. Although this Court has stated that "the specification does not teach that all dry powder inhalers are pulsed inhalation devices," D.I. 96 at 7, the specification need not go that far. The difference in the parties' definitions is that Liquidia's definition would require that pulsed inhalation devices themselves supply the force. But the '327 patent specification describes breath-powered dry powder inhalers—i.e., with no internal force—as example pulsed inhalation devices. It identifies a breath-powered dry powder inhaler as an example pulsed inhalation device and Liquidia's breath-powered Yutrepia™ dry powder inhaler as an example embodiment. *See, e.g.*, Ex. B ('327 patent) at 15:1-9; 21:6-19. There is no basis for Liquidia's apparent conclusion that the inventors intended to require that the device supply force, and thereby exclude from claims 11 and 14 the dry powder inhaler examples identified in the specification.

(i) The intrinsic evidence supports UTC's construction.

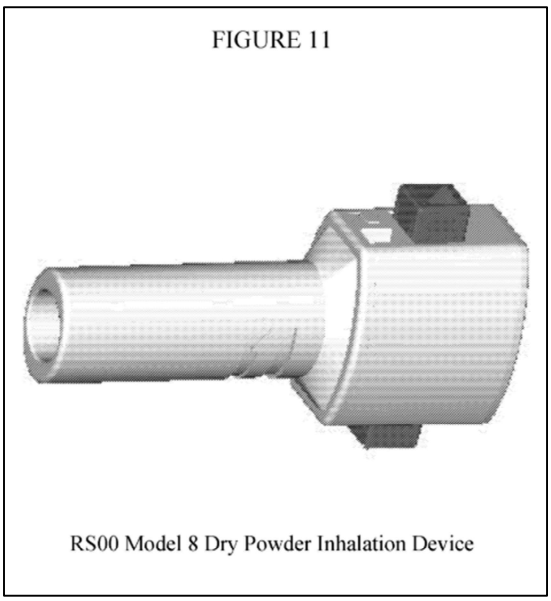
The '327 patent specification describes several categories of "pulsed inhalation device[s]." First, the patent describes a (1) "metered dose inhaler" and (2) "pulsed nebulizer." Ex. B ('327 patent) at 20:48-57; *see also id.*, claims 11-13 (claiming a pulsed inhalation device that is a "nebulizer"). Then, the patent explains that the pulsed inhalation device (3) "may be a dry powder inhaler." *Id.* at 21:6-11; *see also id.*, claim 14 (claiming a pulsed inhalation device that is a dry powder inhaler). Courts have long recognized that the phrase "may be" is permissive language indicating that an example belongs to a category. *See, e.g.*, *Nexeon Ltd. v. EaglePicher Techs. LLC*, 2018 WL 1942199, at *7 (D. Del. Apr. 25, 2018) (recognizing that the phrase "*may be*" is "permissive language" when used in a specification to describe embodiments rather than stating something "is" or "must be" the embodiment included in the invention (emphasis added)). Claim 14 therefore merely narrows the broader category—pulsed inhalation devices, which includes at least three sub-categories—to the dry powder inhaler variety.

The remaining text in that same paragraph in column 21 confirms this reading. The specification cites WO2019/237028 ("Guarneri"), which was "incorporated herein by reference in its entirety," as one example "dry powder inhaler" that is a "pulsed inhalation device." Ex. B ('327 patent) at 21:11-14. Guarneri states that its "dry powder inhaler is a breath-powered inhaler." Ex. C (Guarneri) at 838 ([0023]); *see also id.* at 839-40 ([0027]), 842 ([0038]). To state the obvious, the force in *breath-powered* inhalers is provided by the user, not by the device itself, and therefore the

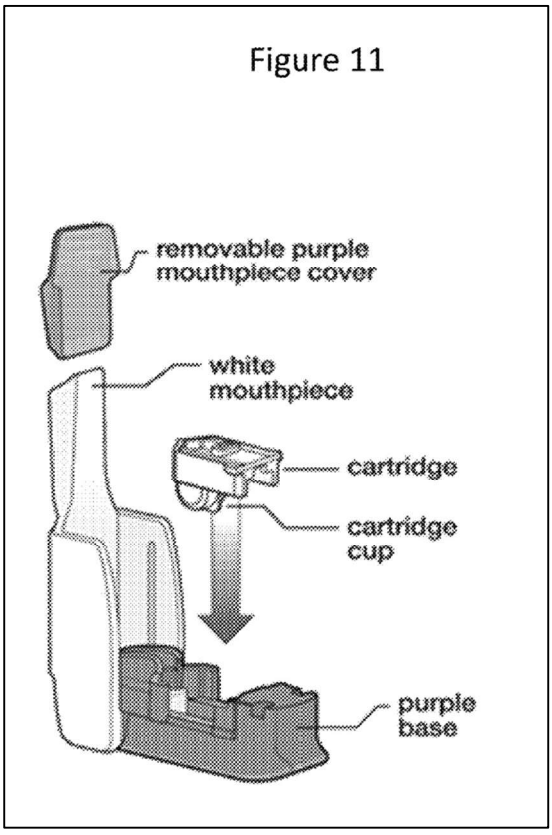
drug is delivered with the patient's breath—not continuously. The '327 patent description of Guarneri's dry powder inhaler as an example "pulsed inhalation device" therefore establishes that breath-powered dry powder inhalers, without any internal means to provide its own force, are "pulsed inhalation devices" within the scope of claims 11 and 14.

The '327 patent also incorporates by reference WO2017/192993 ("Roscigno"), which discloses the administration of treprostinil "using an RS00 Model 8 dry powder inhalation device"—the same breath-powered inhaler used in Liquidia's accused Yutrepia product. *See* Ex. B ('327 patent) at 15:5-9, 54:1-3; Ex. C (Roscigno) at 701 ([0041]), 829 (Fig. 11); D.I. 52 at 13-14; D.I. 54 at 20-21. Figure 11 (reproduced at upper right) is an image of the breath-powered RS00 device, and it does not show any force-providing mechanisms. Ex. C (Roscigno) at 829 (Fig. 11).

The '327 patent (reproduced at right) also depicts a breath-powered dry powder inhaler that



Roscigno Figure 11



'327 patent Figure 11

can be used to administer treprostinil. *See* Ex. B ('327 patent) at 5:66-67, Fig.11.[16]

The dry powder inhalers described in Guarneri, the '327 patent, and Roscigno are breath-powered and therefore provide non-continuous drug delivery with the patient's breath—i.e., "pulses." None have stored energy to provide the force to expel drug powder from the device. Guarneri does not describe its dry powder inhaler as containing "any electronic machinery," nor does it indicate that it could "generate a 'pulse' of inhaled treprostinil" or "generate any energy or power to expel powder from the device." *Cf.* D.I. 96 at 7 (quoting D.I. 54, ¶ 56). Similarly, Figure 11 of the '327 patent shows no machinery for providing a force to deliver inhaled treprostinil. Roscigno likewise makes clear that the force for drug delivery from the RS00 is provided by the patient's breath, not the device itself. Ex. C (Roscigno) at 697 ([0031]), 723 ([00105]), 829 (Fig. 11); *see also id.* at 692 ([0012]), 724 ([00109]). It would be inconsistent with the intrinsic evidence to include a "force" limitation in the construction for this term, and UTC's construction respects the specification by omitting a force limitation.

(ii) Liquidia's proposed construction would exclude embodiments in the specification by importing a limitation from extrinsic evidence.

As previously noted and argued in the preliminary injunction papers, Liquidia has imported the "provides the force for" limitation in an attempt to create a non-infringement defense. But that limitation runs counter to the '327 patent's disclosures. Because the "breath-powered" inhaler described in Guarneri does not provide its own "force" to deliver drug, it would be excluded by Liquidia's proposed construction. As would the devices described in Roscigno and '327 patent, Figure 11. These exclusions demonstrate the error of Liquidia's construction, as courts "normally do not interpret claim terms in a way that excludes disclosed examples in the specification."

[16] The breath-powered inhaler depicted in Figure 11 is described by the '327 patent as the inhaler used to administer treprostinil in the clinical trial of Example 5. Ex. B ('327 patent) at 47:34-39.

Verizon Servs. Corp. v. Vonage Holdings Corp., 503 F.3d 1295, 1305 (Fed. Cir. 2007); *see also Oatey Co. v. IPS Corp.*, 514 F.3d 1271, 1276-77 (Fed. Cir. 2008) (collecting cases and describing precedent as "finding district court's claim construction erroneously excluded an embodiment described in an example in the specification, where the prosecution history showed no . . . disavowal of claim scope").

Moreover, there is nothing in the '327 patent specification that suggests or implies that a pulsed inhalation device must provide its own "force." The disputed term is a "*pulsed* inhalation device," not a "*powered* inhalation device." The term "force" is never used in the '327 patent with respect to the disputed term. *See generally* Ex. B ('327 patent).

In the preliminary injunction proceedings, Liquidia relied on extrinsic evidence for the force limitation: the declaration and testimony of Dr. Channick. Liquidia's reliance on that evidence instead of the specification is both legally and substantively misguided. *E.g.*, *Osram GmbH v. Int'l Trade Comm'n*, 505 F.3d 1351, 1356 (Fed. Cir. 2007) ("The patent specification is the primary resource for determining how an invention would be understood by persons experienced in the field.").

Everything Dr. Channick cites is extrinsic evidence, and even his reliance on "[t]he PAH literature" (D.I. 54, ¶¶ 147-48) is flawed. First, he cites Barst (Ex. 10), a 2012 paper purporting to review pulsed inhaled nitrous oxide delivery systems used in clinical studies of PAH. D.I. 54, ¶ 148. Just because those nitrous oxide *gas* devices used for treating PAH provided force does not mean that all pulsed devices must provide the force to deliver the drug, regardless of drug and disease. As his second and final example, Dr. Channick cited Lee (Ex. 11), a paper published in 2022. Although the Lee reference does relate to treprostinil, it only describes a nebulizer delivery system—not a dry powder inhaler. *Cf. Phillips*, 415 F.3d at 1313. There is no basis to import a

limitation from one pulsed nebulizer reference to the claims of the '327 patent. *See Genuine Enabling Tech. LLC v. Nintendo Co., Ltd.*, 29 F.4th 1365, 1374-75 (Fed. Cir. 2022) (reversing where the claim construction "relied on extrinsic evidence upon extrinsic evidence to draw a bright line in claim scope not suggested anywhere in the intrinsic record.").

* * *

The evidence demonstrates that a pulsed inhalation device includes dry powder inhalers that deliver a drug non-continuously (i.e., in a pulse), whether the device is internally or breath-powered. The Court should reject the "force" limitation Liquidia seeks to import from extrinsic evidence and adopt UTC's construction.

2. Defendant's Answering Position

A fundamental tenet of claim construction is that the claim language must be construed from the perspective of a POSA and that claim terms are generally given their ordinary meaning as understood by a POSA at the time of the invention. *See Phillips*, 415 F.3d at 1313 ("The inquiry into how a person of ordinary skill in the art understands a claim term provides an objective baseline from which to begin claim interpretation."); *InterDigital Commc'ns, LLC v. Int'l Trade Comm'n*, 690 F.3d 1318, 1324 (Fed. Cir. 2012) ("Claim terms are generally given their ordinary meaning as understood by persons skilled in the art in question at the time of the invention. The plain meaning of claim language ordinarily controls unless the patentee acts as his own lexicographer and provides a special definition for a particular claim term[.]") (internal citation omitted).

(i) Liquidia's proposed construction comports with the intrinsic and extrinsic evidence

Here, the evidence shows that a POSA would have understood the plain meaning of "pulsed inhalation device" to mean "a device that provides the force for non-continuous inhaled drug

delivery." To begin with, the '327 patent specification cites several patent applications and patents as examples of pulsed inhalation devices, with each reference disclosing the Optineb® ultrasonic nebulizer which produces a force for non-continuous inhaled drug delivery. '327 patent, 20:53–57 (incorporating by reference U.S. Patent App. Pub. No. 2008/0200449 and U.S. Patent Nos. 9,358,240; 9,339,507; 10,376,525; and 10,716,793 as examples of pulsed inhalation devices); Ex. 12 (U.S. Patent App. Pub. No. 2008/0200449) at [0070] (disclosing the Optineb® ultrasonic nebulizer); Ex. 13 (U.S. Patent No. 9,358,240) at 12:49–50 (same); Ex. 14 (U.S. Patent No. 9,339,507) at 12:57–58, 14:36–39 (same); Ex. 15 (U.S. Patent No. 10,376,525) at 12:57–58, 14:54–57 (same); Ex. 16 (U.S. Patent No. 10,716,793) at 12:58–59, 14:35–38 (same).[17] Additionally, the INCREASE study, which is allegedly the basis for the '327 patent (*see* Ex. 9 at 8:7-10), discloses "administ[ration] by means of an ultrasonic, pulsed-delivery nebulizer[.]" (D.I. 52, Ex. 23 at 325.) Thus, a POSA would understand that the examples in the intrinsic evidence support the definition of "pulsed inhalation device" as "a device that provides the force for noncontinuous inhaled drug delivery."

Additionally, a POSA would understand what the term "pulsed" means. The dictionary definition of the verb "pulse" is (1) "to produce or modulate (something, such as electronic waves) in the form of pulses" or (2) "to cause (an apparatus) to produce pulses[.]" *See* Ex. 17 at 2 (Merriam Webster Dictionary entry dated Oct. 23, 2019). Although a dictionary is considered extrinsic

[17] Each of these patent application publications and patents include the following boilerplate language, but without ever describing dry powder inhalers as a "pulsed inhalation device": "The inhalation device can be also a dry powder inhaler. In such case, the respiratory drug is inhaled in solid formulation, usually in the form of a powder with particle size less than 10 micrometers in diameter or less than 5 micrometers in diameter." Ex. 12 (U.S. Patent App. Pub. 2008/0200449) at [0041]; Ex. 13 (U.S. Patent No. 9,358,240) at 7:18–22; Ex. 14 (U.S. Patent No. 9,339,507) at 7:18–22; Ex. 15 (U.S. Patent No. 10,376,525) at 7:18–22; Ex. 16 (U.S. Patent No. 10,716,793) at 7:22–26.

evidence, here it provides the plain and ordinary meaning of "pulsed" that is entirely consistent with the intrinsic evidence. A POSA would also have been familiar with the PAH literature which indicates that a "pulsed inhalation device" generates a pulse such that it "provides the force for non-continuous inhaled drug delivery." For example, Robyn Barst, et al. reviewed several pulsed inhalation devices used to treat PAH, all of which included a "pulse device." *See* Ex. 10 at 141. Lee, et al. also described "the Tyvaso Inhalation System" as a pulsed inhalation device wherein TD-300/A Tyvaso Inhalation System includes a power supply and delivers inhaled treprostinil over a number of pulses (or "breaths" in the manual). *See* Ex. 11 at 2–3; Ex. 18 at 18–23, 42–45; *see also* D.I. 54, ¶148.

Based on the plain and ordinary meaning of "pulsed," as further supported by the specification of the '327 patent, the term "pulsed inhalation device" should be construed as: "A device that provides the force for non-continuous inhaled drug delivery."

(ii) UTC's proposed construction does not comport with the intrinsic evidence

UTC's proposed construction is inconsistent with how a POSA would understand the word "pulsed" as used in the term "pulsed inhalation device." UTC equates the word "pulsed" with "non-continuous." *See* Opening Br., 41 ("Liquidia agrees that the 'pulsed inhalation device' is a device that provides for non-continuous (*i.e.*, 'pulsed') drug delivery by inhalation."). UTC's expert Dr. Nathan shed additional light on UTC's interpretation of "pulsed inhalation device" and "pulse":

Q: Okay. What, in your opinion, is a pulsed inhalation device?

…

A: One that's not continuous, that it comes out in one pulse

Q: Is the Tyvaso DPI a pulse inhalation device?

…

A: I believe it is regarded as such.

Q: And what is that belief based on?

A: That you actuate it, and it comes out as a pulse while the patient is taking a breath in.

Q: When you say you actuate it, you're equating the breath in with the pulse; is that correct?

…

A: I'm assuming it is.

…

Q: Okay. Sitting here today, you have no knowledge of whether the Yutrepia DPI provides the powder continuously or in pulses in any way; correct?

…

A: My assumption is if it's a dry powder, then it should be pulsed, that's my assumption.

Ex. 19 (Nathan Dep. Tr.) at 130:3-131:2, 135:1–9. To the extent UTC argues, per Dr. Nathan's interpretation, that a "pulsed inhalation device" is "pulsed" because the drug comes out as a pulse while the patient is taking a breath in, such a construction would turn every drug inhalation device into a "pulsed inhalation device." That is, every inhalation device, even continuous delivery devices such as soft mist inhalers, would be "pulsed" because patients only receive the drug when he or she breathes in. This construction is inconsistent with the intrinsic and extrinsic evidence discussed above, and would be contrary to how a POSA would understand the term "pulsed inhalation device." Additionally, because such a construction would encompass every drug inhalation device, it would render the word "pulsed" in the term "pulsed inhalation device" superfluous and cannot be the correct construction. *See Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir. 2005) ("A claim construction that gives meaning to all the terms

of the claim is preferred over one that does not do so."); *Elekta Instrument S.A. v. O.U.R. Sci. Int'l, Inc.*, 214 F.3d 1302, 1307 (Fed. Cir. 2000) (construing claim to avoid rendering a claim limitation superfluous). A breath is not a "pulse" nor is breathing a "pulsed inhalation device."

UTC also points to a single sentence in the '327 patent specification that "a pulsed inhalation device, **may be** a dry powder inhaler[.]" '327 patent, 21:6–14 (emphasis added). Regardless of whether some pulsed inhalation devices "may be" dry powder inhalers, the language of Asserted Claim 14 requires "wherein the pulsed inhalation device **is** a dry powder inhaler. . . ." *Id.* at 54:57–60 (claim 14) (emphasis added)[18]. UTC cites to several patent application publications in its Opening Brief that allegedly disclose a dry powder inhaler that is a pulsed inhalation device. Opening Br., 42–44 (citing WO2019/237028 and WO2017/192993). However, these references, while disclosing dry powder inhalers, do not disclose dry powder inhalers that are pulsed inhalation devices. *Id.*; Ex. 20 (WO2017/192993) at [0011] (disclosing a dry powder inhaler and separately, an "ultrasonic, pulsed nebulization delivery device[,]" but not describing the dry powder inhaler as a "pulsed inhalation device"); Ex. 21 (WO2019/237028) at [0018] (same and not even mentioning the words "pulse" or "pulsed"). The sentence in the '327 patent that "a pulsed inhalation device, may be a dry powder inhaler" alone cannot change the plain meaning of the phrase "***pulsed*** inhalation device," which is fully supported by the intrinsic and extrinsic evidence. *See Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357 (Fed. Cir. 1999) (rejecting patentee's claim construction and vacating a finding of infringement because "us[ing] the written

[18] To show infringement, UTC must establish that Liquidia's dry powder inhaler **is** a pulsed inhalation device. To the extent that UTC argues that because ***some*** pulsed inhalation devices may be dry powder inhalers, then Liquidia's dry powder inhaler must be a pulsed inhalation device, such an infringement theory cannot prevail. At most, the specification suggests that *some* dry powder inhalers could be pulsed inhalation devices. However, that does not mean that *all* dry powder inhalers *are* pulsed inhalation devices.

description to circumvent the plain language of the claim and the clear definition of the disputed claim language found therein was inappropriate."); *White v. Dunbar*, 119 U.S. 47, 51–52 (1886) ("Some persons seem to suppose that a claim in a patent is like a nose of wax, which may be turned and twisted in any direction, by merely referring to the specification, so as to make it include something more than, or something different from, what its words express. … [I]t is unjust to the public, as well as an evasion of the law, to construe [the claim] in a manner different from the plain import of its terms."). And that language certainly cannot transform the plain and ordinary meaning of the term "pulsed" to include any device whether the patient takes in drug by breathing in, as UTC proposes.

3. Plaintiff's Reply Position

The parties agree that a "pulsed inhalation device" must provide non-continuous delivery of inhaled treprostinil to the patient. However, to manufacture an alleged non-infringement position, Liquidia asks the Court to import a "force" limitation—from extrinsic evidence—that would exclude several preferred embodiments from the specification. *Supra* § VI.C.2, at 46-48, 47 n.17, 50 n.18. Liquidia's construction is unsupported and Liquidia's attacks on UTC's construction lack any merit.

Liquidia begins by describing a "fundamental tenet" of claim construction law: that terms must be construed according to how the POSA would understand them. *Id.* at 46. But Liquidia misapplies that standard and ignores two other fundamental tenets: (1) that limitations should not be imported from the specification, and (2) that extrinsic evidence cannot override the language of the claims or the intrinsic evidence. Liquidia violates both.

(i) Liquidia's attempt to import a "force" limitation that is not present in claim 11, claim 14, or the intrinsic evidence should be rejected.

Liquidia reads a "force" limitation into the claims, which violates the "'general proposition[that] a limitation that does not exist in a claim should not be read into that claim.'" *Pfizer Inc. v. Alkem Labs. Ltd.*, 2014 WL 12798743, at *1 n.1 (D. Del. Dec. 2, 2014) (quoting *Biovail Corp. Int'l v. Andrx Pharm., Inc.*, 239 F.3d 1297, 1301 (Fed. Cir. 2001) and holding that the party failed to meet the "sizeable burden" it "fac[ed] . . . in advancing [such a] construction"). Indeed, "[e]ven when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004) (internal quotations omitted). Neither claim 11, claim 14, nor the specification recite anything about force or how a pulse from a pulsed inhalation device must be generated. Liquidia's arguments fall far short of the "demonstrated . . . clear intention" required to limit the scope of the claims.

Liquidia's citation to intrinsic evidence is limited to several patents and a patent application publication (*supra* § VI.C.2, at 46-47), but none of them define a "pulsed inhalation device" as something that provides a force or equates the word "pulsed" with a device being self-powered. *See generally* Exs. 12-16. These references instead merely employ "pulsed" to reflect non-continuous drug delivery, which is consistent with UTC's proposed construction. The '327 patent explains that a pulsed inhalation device, among other things, "may be . . . a metered dose inhaler and/or a pulsed nebulizer," Ex. B ('327 patent) at 20:51-53, and then cites these references as examples *of those devices—i.e.*, as example metered dose inhalers and pulsed nebulizers, Ex. B ('327 patent) at 20:53-5. It is undisputed that metered dose inhalers and pulsed nebulizers are "non-continuous." Whether those cited patents and application explicitly define dry powder inhalers as

"pulsed inhalation devices" is irrelevant to the fact that the specification includes those devices in its definition of pulsed inhalation devices. *Cf. supra* § VI.C.2, at 47 n.17.

What matters here is that the '327 patent teaches that the "pulsed inhalation device," which is undisputedly non-continuous, "may be a dry powder inhaler." Ex. B ('327 patent) at 21:6-11. This makes clear to the POSA that at least some dry powder inhalers must fall within the scope of "pulsed inhalation device." Notably, there is no record evidence of any *continuous* dry powder inhaler or dry powder inhaler that "provides the force." Thus, all known DPIs are non-continuous, and at least the breath-powered examples in the specification must be within the scope of claims 11 and 14.

Liquidia complains that this "single sentence" is not sufficient disclosure. *Supra* § VI.C.2, at 50 (citing '327 patent at 21:6-14). But the specification's very next sentence points to a real-world example of a dry powder inhaler that is a "pulsed inhalation device." Ex. B ('327 patent) at 21:11-14. That example—Guarnieri (WO2019/237028)—describes a breath-powered dry powder inhaler. *Supra* § VI.C.1, at 42-43; Ex. C (Guarneri) at 838 ([0023]). The specification includes additional exemplary embodiments of breath-powered dry powder inhalers that can be used in the claimed methods, including in FIG. 11 and Roscigno, which is incorporated by reference. *Supra* § VI.C.1, at 43-44; Ex. B ('327 patent) at 15:5-9, 54:1-3; Ex. C (Roscigno) at 701 ([0041]). Accordingly, the POSA reading the '327 patent would understand that a dry powder inhaler powered by a patient's breath is within the scope of the claimed "pulsed inhalation device." *Supra* § VI.C.1, at 44.

Liquidia's attempt to distinguish Guarneri and Roscigno fails. *Supra* § VI.C.2, 50-51. Those references do not need to use any magic words or expressly define their DPIs as "pulsed

inhalation devices." The '327 patent specification cites those references as DPI examples of a "pulsed inhalation device," and that is enough.

Liquidia's misguided attempt to exclude from the claims what the patent provides as an exemplary embodiment is highlighted by Liquidia's expert, Dr. Channick, who admitted at his deposition that he had never encountered a pulsed inhalation device that is also a dry powder inhaler according to Liquidia's definition. Ex. 23 (Channick Depo Tr.) at 173:18-21. To reiterate, Dr. Channick is unaware of pulsed inhalation devices that fit Liquidia's definition. Liquidia's position appears to be that the POSA would ignore the citations to Guarneri and Roscigno and instead conclude that the only type of dry powder inhaler that would fall within the scope of claims 11 and 14 is a purely hypothetical device. That is nonsense. The law is clear: constructions that exclude preferred embodiments are rarely, if ever, correct. *E.g.*, *CUPP Computing AS v. Trend Micro Inc.*, 53 F.4th 1376, 1381-82 (Fed. Cir. 2022) ("We require highly persuasive evidence to read claims as excluding a preferred embodiment of the invention.") (internal quotations omitted). Indeed, this Court consistently cautions that "'a claim interpretation that would exclude the inventor's device is rarely the correct interpretation.'" *Otsuka Pharm. Co. v. Lupin Ltd.*, 2022 WL 2952759, at *2 (D. Del. July 26, 2022) (citing *Osram GmbH*, 505 F.3d at 1358).

(ii) Liquidia's extrinsic evidence cannot, and does not, override the intrinsic evidence to define "pulsed inhalation device."

Liquidia's extrinsic evidence—which in Liquidia's own words has "little to no probative value on claim construction"[19]—and other arguments are even weaker than its attempts to cite intrinsic support.

[19] Ex. 24 (Letter from Liquidia to UTC) at 6 (Aug. 2, 2024) (referring to UTC's request for documents "that reflect Liquidia's **use** of any claim terms") (emphasis original).

Liquidia first cites extrinsic evidence—the Merriam-Webster dictionary. *Supra* § VI.C.2, at 47-48. As an initial matter, the practice of using dictionary definitions to construe individual parts of a compound claim term is generally disfavored, especially if the specification provides its own definition. *See Align Tech., Inc. v. 3Shape*, 2021 WL 2320139, at *12 (D. Del. June 7, 2021) (citing *Network Com., Inc. v. Microsoft Corp.*, 422 F.3d 1353, 1360 (Fed. Cir. 2005) (holding that "combin[ing] individual dictionary definitions" to compound term's components was "not a tenable theory in light of the specification")). And even if the dictionary should be relied upon, there is no basis to rely only upon Liquidia's cherry-picked definitions. Liquidia presented the dictionary as if it provided two and only two definitions for "pulse"; in reality, there are closer to ten. Ex. 17 at 2. And one that Liquidia conspicuously ignored defines a "pulse" as "a dose of a substance especially when applied over a short period of time," and provides as an example, "pulses of intravenous methylprednisolone." *Id.*; *see also* https://www.merriam-webster.com/dictionary/pulse (more easily readable). UTC's construction is consistent with the dictionary. Meanwhile, neither Liquidia's cited definitions nor the more pertinent definition related to drug delivery define "pulse" as requiring a device to generate a force.

Liquidia also cites Barst and Lee[20] references (extrinsic evidence) as alleged support for the notion that a pulsed inhalation device must itself "provide the force for non-continuous drug delivery." *Supra* § VI.C.2, at 47-48. The term "pulsed inhalation device" appears in neither reference and the '327 patent does not cite to them at all, let alone as examples of the claimed pulsed inhalation device. Barst and Lee use "pulsed" merely to refer to a *non-continuous mode* of drug delivery, not the mechanism or "force" behind that delivery.

[20] Lee was published after the priority date of the '327 patent.

In addition to Barst and Lee, Liquidia also cited Dr. Channick one time, without mentioning him by name, in a "*see also*" cite. *Supra* § VI.C.2, at 48 (citing D.I. 54, ¶ 148); *see Bial-Portela & CA. S.A. v. Alkem Labs. Ltd.*, 2022 WL 4244989, at *25 n.10 (D. Del. Sept. 15, 2022) ("declin[ing] to entertain [a] cursory argument made in passing"). In that paragraph, Dr. Channick describes the Barst and Lee papers and draws a mistaken conclusion regarding what the POSA would understand from unidentified "PAH literature." D.I. 54, ¶ 148. His reasoning and Liquidia's reliance on it are flawed, as the POSA would not infer and import force-generation limitations from the extrinsic Barst and Lee documents. *Network Com., Inc.*, 422 F.3d at 1361-62 (holding that "expert testimony at odds with the intrinsic evidence must be disregarded"). Dr. Channick's conclusory opinion cannot contradict the intrinsic evidence and nothing cited by Liquidia shows a clear intention by the inventors to narrow claim 14 to *powered* dry powder inhalers only.

Finally, Liquidia misrepresents both UTC's position and Dr. Nathan's deposition testimony to assert that UTC's construction would include "every drug inhalation device," "even continuous devices," and thus render the word "pulsed" superfluous. *Supra* § VI.C.2, at 48-50. This is a straw man. Liquidia acknowledges that the phrase "non-continuous inhaled drug delivery" in UTC's construction reflects the meaning that "pulsed" imparts to "pulsed inhalation device." *Id.* at 48. Dr. Nathan also testified that pulsed inhalation devices are those that are "not continuous" and that "[the drug] comes out in one pulse." *Id.* at 48-49. Thus, UTC's proposed construction expressly excludes continuous devices by requiring *non-continuous* inhaled drug delivery."

* * *

Nearly every claim construction case recites the principle that limitations should not be imported from the specification. The claims control. Yet here, Liquidia seeks to import a limitation

from extrinsic evidence—which Liquidia labels as having "little to no probative value"—solely to manufacture an alleged non-infringement position. Only UTC's construction comports with the intrinsic evidence. Liquidia's unsupported proposed construction should be soundly rejected.

4. Defendant's Sur-Reply Position

UTC admits that "some" DPIs fall within the scope of pulsed inhalation device. Reply, 52. But UTC's construction makes ***all*** dry powder inhalers, and in fact ***all*** inhalation devices, pulsed inhalation devices, because UTC admits that a patient's breathing satisfies the non-continuous limitation of its construction. *See, e.g.*, Reply, 53 ("the POSA reading the '327 patent would understand that a dry powder inhaler powered by a patient's breath is within the scope of the claimed 'pulsed inhalation device.'"). UTC's broad definition is unsupported and already rejected. This Court determined that "the specification does not teach that all dry powder inhalers are pulsed inhalation devices. I disagree with Plaintiff that the inventors have relied on lexicography to define dry powder inhalers and pulsed inhalation devices." *See* D.I. 96, 7. Consistent with the specification, Liquidia's construction properly distinguishes between those inhalation devices that are pulsed and those that are not.

UTC claims that Liquidia is "read[ing] a 'force' limitation into the claim[.]" Reply, 51–53. Rather, Liquidia's construction provides the plain and ordinary meaning for how a POSA would understand the term "pulsed" inhalation device. Contrary to precedent, UTC's construction, and its contention that the act of breathing satisfies the "pulsed" limitation, renders this limitation meaningless since all inhalation devices require breathing/inhalation for drug administration. *See Merck*, 395 F.3d at 1372; Response, 48–51.

UTC asserts that the patents and patent publication Liquidia cites from the intrinsic evidence do not "define a 'pulsed inhalation device' as something that provides a force or equates

the word 'pulsed' with a device being self-powered."[21] Reply, 52. UTC also argues, without explanation or support, that "[t]hese references instead merely employ 'pulsed' to reflect non-continuous drug delivery[.]" *Id.* UTC is wrong. The references show "pulsed inhalation devices" "provides the force for non-continuous inhaled drug delivery." For example, one reference discloses an embodiment where "[a] pulse of aerosol was **generated** every 6 seconds." Ex. 12, [0023] (emphasis added). The same reference discloses that "[a]ll inhalations were performed with the Optineb® ultrasonic nebulizer (Nebutec, Elsenfeld, Germany)" and that the "aerosol was **generated** by a pulsed ultrasonic nebulizer (Ventaneb, Nebutec, Elsenfeld, Germany) in cycles consisting of 2 seconds **aerosol production (pulse)** and 4 seconds pause." *Id.*, [0070], [0074] (emphasis added). Indeed, both the Optineb® and Ventaneb® manuals disclose a power supply and programs that generate a pulse of aerosolized drug (e.g., by alternating between an active phase of nebulizing treprostinil and a passive phase). Ex. 26, 14–15, 20–21; Ex. 27, 37–42. The remaining references that Liquidia cites from the intrinsic evidence all include similar disclosures that show "pulsed inhalation devices" generate a pulse because the device "provides the force for non-continuous inhaled drug delivery." *See generally* Exs. 13–16. These references also separately disclose dry powder inhalers, but do not equate them to pulsed inhalation devices. *See* Exs. 12-16; Response, 47 n.17.

UTC relies on the Guarneri and Roscigno references, but neither support UTC's construction. *See* Reply, 53. Liquidia previously explained that both references do provide examples of pulsed inhalation devices—an "ultrasonic, pulsed nebulization delivery device" in Roscigno and the Optineb® ultrasonic nebulizer in Guarneri. Response, 50–51. Separately, both

[21] Liquidia reiterates that these references also never describe dry powder inhalers as a "pulsed inhalation device." *See* Response, 47 n.17.

references also disclose dry powder inhalers, but neither reference equates a dry powder inhaler to a pulsed inhalation device. *Id.* Therefore, a POSA would understand that neither of these references cited in the '327 patent specification specifically describe dry powder inhalers that are pulsed inhalation devices.

Liquidia is not seeking to exclude an exemplary embodiment. *See* Reply, 53–54. Liquidia does not dispute that a dry powder inhaler that meets Liquidia's construction would be a pulsed inhalation device. That Dr. Channick has not encountered a dry powder inhaler that is a pulsed inhalation device is irrelevant.[22] What is relevant for claim construction is that UTC cannot now exclude the term "pulsed" from its claimed inhalation device.

Finally, UTC criticizes Liquidia's use of extrinsic evidence, but Liquidia merely cites to the extrinsic evidence as providing additional clarity that its proposed construction is consistent with how a POSA understands the plain and ordinary meaning of "pulsed"—a term which UTC seeks to read out of the claimed pulsed inhalation device. *See* Response, 50–51. Thus, Liquidia's extrinsic evidence is proper.

[22] UTC mischaracterizes Dr. Channick's testimony. Reply, 54. When asked whether he "encountered a pulse inhalation device that is also a dry powder inhaler[,]" Dr. Channick answered "No, not in my experience." Ex. 23, 173:18-21.

MORRIS, NICHOLS, ARSHT & TUNNELL LLP

/s/ Michael J. Flynn

Michael J. Flynn (#5333)
1201 North Market Street
P.O. Box 1347
Wilmington, DE 19899
(302) 658-9200
mflynn@morrisnichols.com

Attorneys for Plaintiff United Therapeutics Corporation

OF COUNSEL

William C. Jackson
Katherine Cheng
GOODWIN PROCTER LLP
1900 N St. NW
Washington, DC 20036
(202) 346-4000

Eric T. Romeo
Louis L. Lobel
GOODWIN PROCTER LLP
100 Northern Avenue
Boston, MA 02210
(617) 570-1000

Adam J. Horowitz
GOODWIN PROCTER LLP
The New York Times Building
620 Eighth Avenue
New York, NY 10018
(212) 813-8800

Douglas Carsten
Art Dykhuis
Katherine Pappas
MCDERMOTT WILL & EMERY LLP
18565 Jamboree Road, Suite 250
Irvine, CA 92615
(949) 851-0633

SHAW KELLER LLP

/s/ Karen E. Keller

Karen E. Keller (No. 4489)
Nathan R. Hoeschen (No. 6232)
Emily S. DiBenedetto (No. 6779)
I.M. Pei Building
1105 North Market Street, 12th Floor
Wilmington, DE 19801
(302) 298-0700
kkeller@shawkeller.com
nhoeschen@shawkeller.com
edibenedetto@shawkeller.com

OF COUNSEL:

Sanya Sukduang
Phillip E. Morton
Jonathan Davies
Adam Pivovar
Rachel Preston
Rosalyn D. Upton
COOLEY LLP
1299 Pennsylvania Avenue, NW, Suite 700
Washington, DC 20004-2400
(202) 842-7800

Lauren Strosnick
Kyung Taeck Minn
COOLEY LLP
3175 Hanover Street
Palo Alto, CA 94304-1130
(650) 843-5000

Attorneys for Defendant Liquidia Technologies, Inc.

August 29, 2024